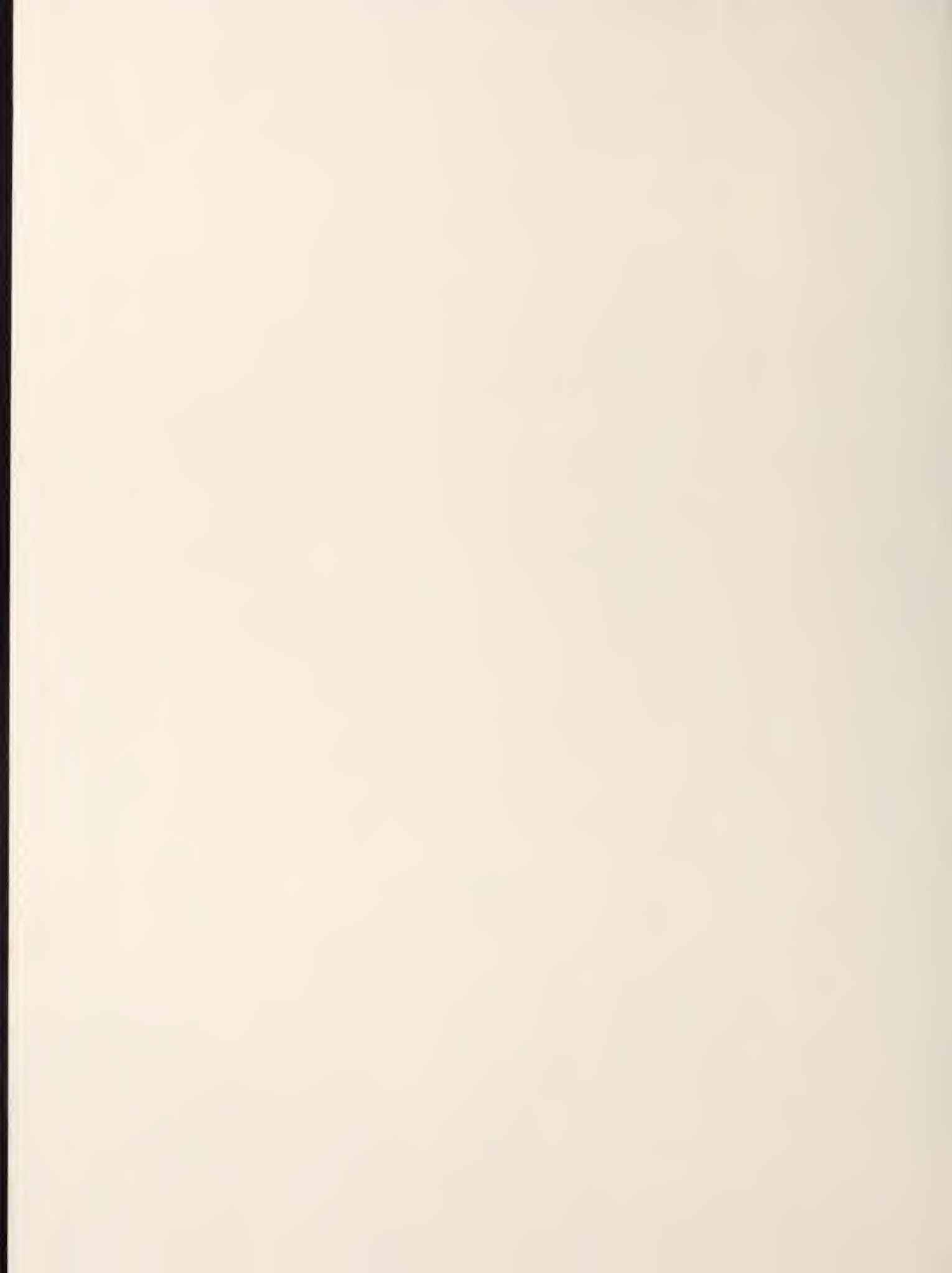


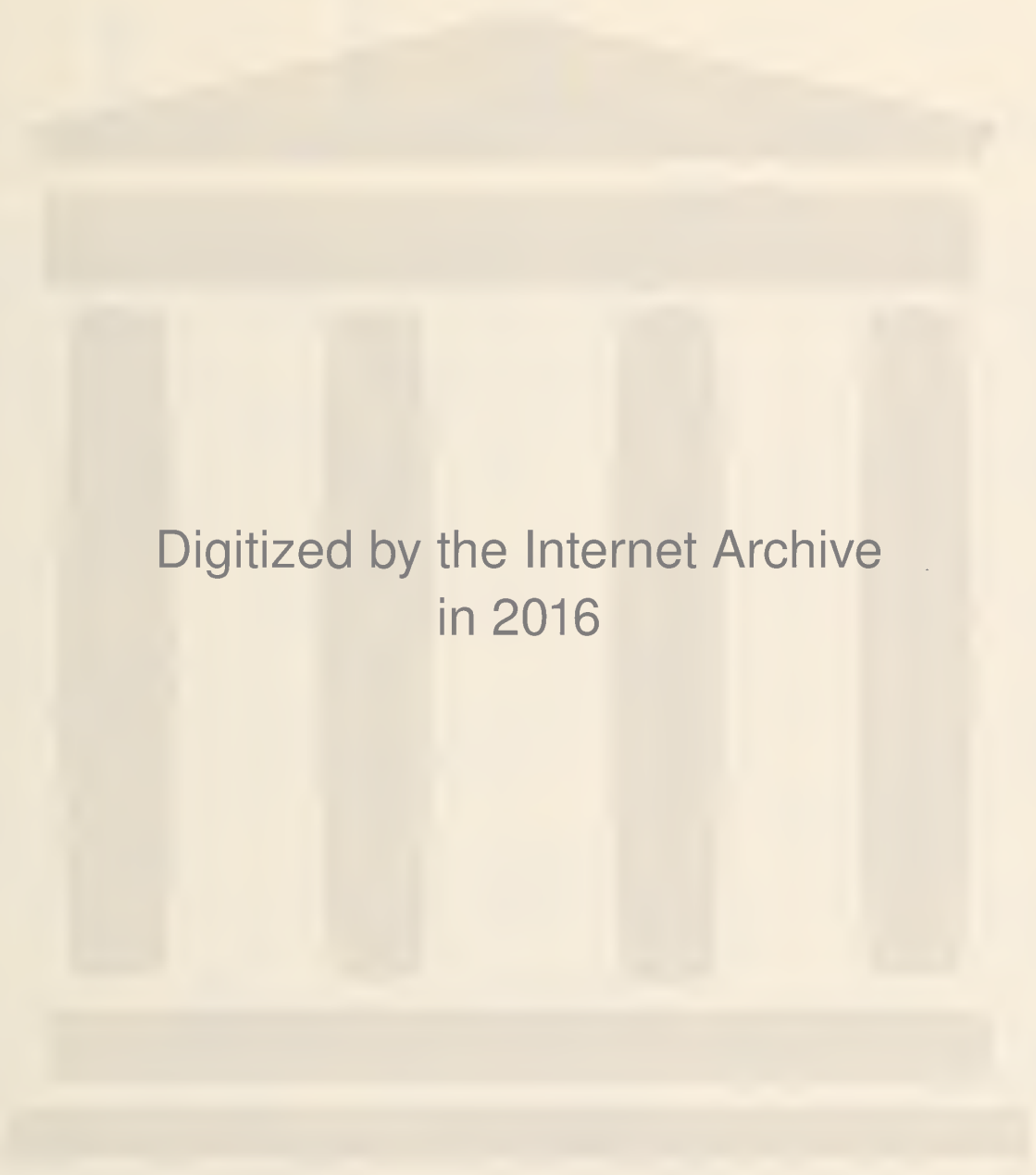
The New York
Academy of Medicine



By Exchange







Digitized by the Internet Archive
in 2016

<https://archive.org/details/newyorkstatejour93unse>

LIBRARY
JUL 13 1993
NEW YORK ACADEMY
OF MEDICINE

New York State Journal of Medicine



VOL 93
NO 1
JANUARY
1993

**HEALTH CHALLENGES FOR
THE 1990s**

**THE STATUS OF THE NEW
YORK STATE JOURNAL OF
MEDICINE**

**AIDS MORTALITY AMONG
RESIDENTS OF PUERTO
RICO AND AMONG PUERTO
RICAN IMMIGRANTS AND
OTHER HISPANIC RESIDENTS
OF NYC, 1981-1989**

**ANTI-CONVULSANT DRUGS,
SMOKING, AND BODY
WEIGHTS IN PSYCHIATRIC
IN-PATIENTS**

**MEDICARE HOSPITAL
MORTALITY: HOW DOES
NYS COMPARE?**

**ETHICAL AND SOCIAL
ISSUES IN ORGAN
PROCUREMENT FOR
TRANSPLANTATION**

We don't
believe
one loss
should
automatically
lead to
another.

Being accused of professional negligence in your treatment of a patient is bad enough. For a medical liability company to compound the charge by automatically cancelling or surcharging your policy is grossly unfair. Unfortunately, some insurers consider even one claim (no matter how unfounded) as reason enough to cancel your coverage.

At MLMIC*, we treat policyholders better than that. We won't cancel or surcharge a policy on the basis of claims history without first submitting it for review to a panel of consulting physicians. Because of the success and strength of our Cooperative Peer Review system, the New York State Insurance Department does not require MLMIC to use an automatic surcharge schedule. *We are the only medical liability carrier in the state with this advantage.*

MLMIC also has the country's largest and most experienced professional liability claims department, as well as New York State's largest risk management department.

Call 1-800-ASK-MLMI (metro) or 1-800-356-4056 (upstate) for more information and an application.

*The only medical liability insurer approved by the Medical Society of the State of New York. Physicians protecting physicians since 1975.



PROFESSIONAL LIABILITY INSURANCE POLICY

(Claims Made Form)

DPIC

Doctors Protective
Insurance Company

CANCELLED

NOTICE
This policy provides coverage limited to claims made against you for professional services you have provided, in the course of your practice. You must have provided professional services on or after the retroactive date and before the end of the policy period during the policy period or within 60 days following termination of the policy. Please read your entire policy, as it contains numerous interrelated sections and

MLMISC

Medical Liability
Mutual Insurance Company

Our defense never rests.

250 Harrison St., Syracuse, NY 13202 • 315-428-1188
2 Park Ave., New York, NY 10016 • 212-576-9800
90 Merrick Ave., East Meadow, NY 11554 • 516-794-7200

FREEDOM FROM PAIN!

**Extra strength pain relief
free of extra prescribing
restrictions.**

- Telephone prescribing in most states
- Up to five refills in 6 months
- No triplicate Rx required

**15 years of proven
clinical experience**

- Effective central and peripheral pain relief.
- Excellent patient acceptance—nausea, sedation and constipation have rarely been reported.¹
- Four to six hours of extra strength pain relief from a single dose.
- The heritage of VICODIN[®]* — over one billion doses prescribed.²
- The 8th most frequently prescribed medication in America.²

vicodin ES 

(hydrocodone bitartrate 7.5mg [Warning: May be habit forming]
and acetaminophen 750mg)

**Extra strength pain relief
you can phone in.**

¹ Data on file, Knoll Pharmaceutical Company

² Standard industry new prescription audit.

* (hydrocodone bitartrate 5mg [Warning: May be habit forming] and acetaminophen 500 mg)



Maintain control of your patient's pain therapy.

R_x
Specify

*Do not
substitute*

vicodin ES

(hydrocodone bitartrate 7.5mg (Warning: May be habit forming)
and acetaminophen 750mg)

It's your prescription— not a suggestion.

INDICATIONS AND USAGE: For the relief of moderate to moderately severe pain. **CONTRAINDICATIONS:** Hypersensitivity to acetaminophen or hydrocodone. **WARNINGS:** **Respiratory Depression:** At high doses or in sensitive patients, hydrocodone may produce dose-related respiratory depression. **Head Injury and Increased Intracranial Pressure:** The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a preexisting increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries. **Acute Abdominal Conditions:** The administration of narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions. **PRECAUTIONS:** **Special Risk Patients:** VICODIN/VICODIN ES Tablets should be used with caution in elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture. **Cough Reflex:** Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when VICODIN/VICODIN ES Tablets are used postoperatively and in patients with pulmonary disease. **Drug Interactions:** Patients receiving other narcotic analgesics, antipsychotics, anxiolytic agents, or other CNS depressants (including alcohol) concomitantly with VICODIN/VICODIN ES Tablets may exhibit an additive CNS depression. The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone. The concurrent use of anticholinergics with hydrocodone may produce paralytic ileus. **Usage in Pregnancy:** **Teratogenic Effects:** Pregnancy Category C. Hydrocodone has been shown to be teratogenic in hamsters when given in doses 700 times the human dose. There are no adequate and well-controlled studies in pregnant women. VICODIN/VICODIN ES Tablets should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nonteratogenic effects:** Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting, and fever. **Labor and Delivery:** Administration of VICODIN/VICODIN ES Tablets to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used. **Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from VICODIN/VICODIN ES Tablets, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use:** Safety and effectiveness in children have not been established. **ADVERSE REACTIONS:** The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients and some of these adverse reactions may be alleviated if the patient lies down. Other adverse reactions include: **Central Nervous System:** Drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, psychic dependence and mood changes. **Gastrointestinal System:** The antiemetic phenothiazines are useful in suppressing the nausea and vomiting which may occur (see above); however, some phenothiazine derivatives seem to be antianalgesic and to increase the amount of narcotic required to produce pain relief, while other phenothiazines reduce the amount of narcotic required to produce a given level of analgesia. Prolonged administration of VICODIN/VICODIN ES Tablets may produce constipation. **Genitourinary System:** Ureteral spasm, spasm of vesical sphincters and urinary retention have been reported. **Respiratory Depression:** Hydrocodone bitartrate may produce dose-related respiratory depression by acting directly on the brain stem respiratory center. Hydrocodone also affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing. If significant respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride. Apply other supportive measures when indicated. **DRUG ABUSE AND DEPENDENCE:** VICODIN/VICODIN ES Tablets are subject to the Federal Controlled Substance Act (Schedule III). Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, VICODIN/VICODIN ES Tablets should be prescribed and administered with caution. **OVERDOSAGE:** **Acetaminophen Signs and Symptoms:** In acute acetaminophen overdose, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma, and thrombocytopenia may also occur. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion. **Hydrocodone Signs and Symptoms:** Serious overdose with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdose, apnea, circulatory collapse, cardiac arrest and death may occur.

Revised March 1992

5890

Knoll Pharmaceutical Company
30 North Jefferson Road
Whippany, New Jersey 07981

BASF Group



New York State Journal of Medicine



COMMITTEE ON PUBLICATIONS, LIBRARY, AND ARCHIVES

MILTON GORDON, MD, Chairman

PHILIP P. BONANNI, MD, Vice-Chairman

JOSEPH I. COHN, MD

SHARON C. HERMAN MEAD, MD

JONATHAN A. HYDE (*Medical student*)

JOSEPH F. MURATORE, MD

STANLEY LUFTSCHEIN, MD

DONNA B. O'HARE, MD

JOHN T. PRIOR, MD

Editor	PASCAL JAMES IMPERATO, MD
Consulting Editor	JOHN T. FLYNN, MD
Consulting and Book Review Editor	RICHARD B. BIRRER, MD
Consulting Editor	NAOMI R. BLUESTONE, MD, MPH
Consulting Editor	CARL POCHEDLY, MD
Consultant in Biostatistics	JOSEPH G. FELDMAN, DRPH
Managing Editor	RALPH W. BATTEY
Advertising Production Coordinator	KEVIN DAVEY
Copy Editor	VICKI GLASER
Editorial Assistant	MARYANN VIGLIOTTI
Administrative Assistant	MAUREEN MAHER
Librarian	ELLA ABNEY

ASSOCIATE EDITORIAL BOARD 1993

RANDALL BLOOMFIELD, MD	FLORENCE KAVALER, MD
ROBERT D. BRANDSTETTER, MD	JAMES M. MORRISSEY, ESQ
JOHN S. DAVIS, MD	STEPHEN NORDLICHT, MD
CHARLES D. GERSON, MD	JOSEPH SCHLUGER, MD
MYLES S. GOMBERT, MD	RICHARD A. STEIN, MD
ALFRED P. INGEGNO, MD	RODRIGO E. URIZAR, MD
ARTHUR H. WOLINTZ, MD	

Microform copies. This publication is available on microform film. Address orders to University Microfilms, 300 North Zeeb Road, Ann Arbor, MI 48106.

Advertising representatives. *Pharmaceutical Advertising:* Cunningham Associates, PO Box 308, Park Ridge, NJ 07656. Telephone: (201) 767-4170. *Non-Pharmaceutical Advertising:* Cookson Media Services, Inc., PO Box 3669, Trenton, NJ 08629. Telephone: (609) 393-7196.

MEDICAL SOCIETY OF THE STATE OF NEW YORK

MORTON M. KURTZ, MD,	<i>President</i>
STANLEY A. STECKLER, MD,	<i>President-Elect</i>
CHARLES N. ASWAD, MD,	<i>Past-President</i>
JAMES H. COSGRIFF, JR, MD,	<i>Vice-President</i>
GEORGE LIM, MD,	<i>Secretary</i>
JOYCE M. MCCHESNEY, MD,	<i>Assistant Secretary</i>
ANTONIO F. LASORTE, MD,	<i>Treasurer</i>
STANLEY L. GROSSMAN, MD,	<i>Assistant Treasurer</i>
SEYMOUR R. STALL, MD,	<i>Speaker</i>
JOHN H. CARTER, MD,	<i>Vice-Speaker</i>

Councilors

Term Expires 1993

RANDALL D. BLOOMFIELD, MD,	Kings
WILLIAM A. DOLAN, MD,	Monroe
ROBERT M. GEORGE, MD,	Oneida
STUART I. ORSHER, MD,	New York

Term Expires 1994

ROBERT BRUCE BERGMANN, MD,	Nassau
RICHARD A. HUGHES, MD,	Warren
JEFFREY A. RIBNER, MD,	Broome
ANTHONY P. SANTOMAURO, MD,	Erie

Term Expires 1995

BRUCE H. BERLIN, MD,	Suffolk
ALBERT M. ELLMAN, MD,	Albany
FRED N. FLATAU, MD,	Queens
SANFORD A. KAPLAN, MD,	Westchester

Resident Councilor (representing the Resident Physician Section)

PAUL PIPIA, MD, New York

Student Councilor (representing the Medical Student Section)

LEON HENDERSON, New York

Trustees

JAMES M. FLANAGAN, MD,	Wayne
(Chairman)	
JOHN A. FINKBEINER, MD,	New York
SAMUEL M. GELFAND, MD,	Nassau
M. THEODORE TANENHAUS, MD,	Kings
CHARLES D. SHERMAN, JR, MD,	Monroe
DUANE M. CADY, MD,	Onondaga
ROBERT A. MAYERS, MD,	Westchester

Executive Vice-President	DONALD F. FOY
Deputy Executive Vice-President	WILLIAM R. EGAN
Executive Vice-President Emeritus	GEORGE J. LAWRENCE, JR, MD
Program Director, Committee for Physicians' Health	LINDA A. LAMBERT
Director, Division of Communications	THOMAS M. DONOGHUE
Director, Division of Finance and Administration	PHILIP A. SCHUH, CPA
General Counsel	DONALD R. MOY, ESQ
Director, Division of Governmental Affairs	GERARD L. CONWAY, ESQ
Director, Division of Management Information Services	GEORGE J. ADJAMI
Director, Division of Marketing and Meeting Services	GERALD SULLIVAN
Director, Division of Membership Support Services	EUNICE M. SKELLY
Director, Division of Planning, Research, and Development	MICHAEL W. DELANEY, CAE
Director, Division of Policy Coordination	IRMA A. ERICKSON
Director, Division of Public Health and Education	PETER B. FARNSWORTH, MD
Director, Division of Scientific Publications	PASCAL JAMES IMPERATO, MD
Director, Division of Socio-Medical Economics	MARIO V. MENGHINI
Consultant	EDWARD SIEGEL, MD

The New York State Journal of Medicine (ISSN 0028-7628) is published monthly by the Medical Society of the State of New York. Copyright © 1993, Medical Society of the State of New York. Material may be photocopied for noncommercial scientific or educational use only. Special arrangements and permission are required from the author(s) of the particular article and from the editor for any other purpose. The editors of the *Journal* assume no responsibility for opinions and claims expressed in the articles contributed by individual authors.

SUBSCRIPTION INFORMATION. The annual subscription for members (\$30.00) is included in the annual membership dues. The subscription rate to nonmembers in the United States and Canada is \$40.00 (\$45.00 for all other countries). The single copy rate is \$6.00 Domestic/Canada, and \$7.00 Foreign, except for special issues. This includes postage. Change of address requests should give both the old and new address and allow six weeks for changeover.

The address for EDITORIAL, CIRCULATION, and ADVERTISING OFFICES is PO Box 5404, Lake Success, New York 11042. Telephone: (516) 488-6100.

POSTAGE. Second class postage is paid at New Hyde Park, New York, and additional mailing office. POSTMASTER: Send POD Form 3579 to New York State Journal of Medicine, PO Box 5404, Lake Success, New York 11042.

New York State Journal of Medicine

JANUARY 1993 / Volume 93, Number 1



Contents

COMMENTARIES

- 1 **Health challenges for the 1990s**
MARK R. CHASSIN, MD, MPH
- 4 **Cost containment and academic medicine**
JORDAN J. COHEN, MD; JULES COHEN, MD; ALBERT S. KUPERMAN, MD;
ANTHONY P. TARTAGLIA, MD; FRANK JONES
- 7 **The status of the *New York State Journal of Medicine*: Where are we?**
MILTON GORDON, MD

RESEARCH PAPERS

- 12 **Trends in AIDS mortality among residents of Puerto Rico and among Puerto Rican immigrants and other Hispanic residents of New York City, 1981-1989**
BARBARA S. MENENDEZ, PhD; STEVE BLUM, PhD; TEJINDER P. SINGH, PhD; ERNEST DRUCKER, PhD
- 16 **Anti-convulsant drugs, smoking, and body weights in psychiatric in-patients**
BHARAT S. SHAH, MD, HAROLD RATNER, MD
- 18 **State experience with Medicare hospital mortality: How does New York State compare?**
JOE FEINGLASS, PhD; LARRY MANHEIM, PhD; STEPHEN SHORTELL, PhD;
EDWARD F. X. HUGHES, MD, MPH

THE CPC

- 22 **Sudden death after acute myocardial infarction**
JOHN T. FLYNN, MD

COMMITTEE REPORT

- 30 **Ethical and social issues in organ procurement for transplantation**
FRED ROSNER, MD; JOHN B. HENRY, MD; JONATHAN R. WOLPAW, MD; PETER P. SORDILLO, MD, PhD; PHILIP H. SECHZER, MD; PETER ROGATZ, MD; HERMAN M. RISEMBERG, MD; FERNANDO V. ONA, MD; PATRICIA J. NUMANN, MD; ROBERT E. LOWENSTEIN, MD, PhD; LAURENCE LOEB, MD; ALLISON B. LANDOLT, MD;
PIETER R. KARK, MD; ABRAHAM L. HALPERN, MD; PETER B. FARNSWORTH, MD;
ERIC J. CASSELL, MD; ANTHONY BUSCAGLIA, MD; ALLEN J. BENNETT, MD

(continued on p 5A)



HISTORY

- 35 The story of Lassa fever—Part IV: The politics of research**
JOHN D. FRAME, MD
- 41 Scientific failure in an age of optimism: Public reaction to Robert Koch's tuberculin cure**
DAVID LEIBOWITZ, MD

SPECIAL ARTICLES

- 49 Molecules and magnets**
LOIS GREENE STONE
- 50 Psychic advisor**
NAOMI BLUESTONE, MD

CASE REPORTS

- 54 Mediastinal teratoma presenting as empyema**
HERBERT H. SCHERZER, MD; KAUSHIK J. PATEL, MD; JOHN J. VOTTO, DO;
LOUIS BROWN, MD
- 55 Missed diagnosis of acute arthritic gout in kidney transplant recipients**
INDRA D. DANIELS, MD; ELI A. FRIEDMAN, MD
- 57 Supraventricular tachycardia induced by swallowing**
LAWRENCE GOULD, MD
- 58 Morgagni hernia mimicking a lipomatous tumor**
PERRY S. GERARD, MD; ERIC WILCK, MD; ELLIOT SENDEROFF, MD;
STUART GOLBEY, MD
- 59 Transitional cell carcinoma of the renal pelvis in an incompletely duplicated collecting system**
DANILO ASASE, MD; RONALD G. FRANK, MD; PERRY S. GERARD, MD; KRIS LINDSAY, MD; GILBERT J. WISE, MD

LETTERS TO THE EDITOR

- 62 The value of the *New York State Journal of Medicine***
ALFRED GELLHORN, MD
- 62 Distress over attempts to discontinue the *New York State Journal of Medicine***
ABRAHAM L. HALPERN, MD
- 62 The need to continue publishing the *New York State Journal of Medicine***
RICHARD D. LEVERE, MD
- 62 High regard for the *New York State Journal of Medicine***
PETER ROGATZ, MD

(continued on p 6A)



- 62 **Praise for the quality of the *New York State Journal of Medicine***
CHRISTOPHER HOOLIHAN
- 63 **Support for the *New York State Journal of Medicine***
RABBI LEVI MEIER, PhD
- 63 **Support for continuing the *New York State Journal of Medicine* as a peer-reviewed clinical and scientific publication**
BERNARD J. PISANI, MD
- 63 **Thanks from the Committee on Publications, Library, and Archives for support of the *New York State Journal of Medicine***
MILTON GORDON, MD
- 63 **Regulated medical waste: Is any of it infectious?**
ANTONIO BOBA, MD, SEAN F. X. DUGAN, LLM

ESSAY REVIEW

- 65 **Medical writing**
NAOMI BLUESTONE, MD

67 BOOK REVIEWS

- 70 GUIDELINES TO AUTHORS

HOUSE OF DELEGATES

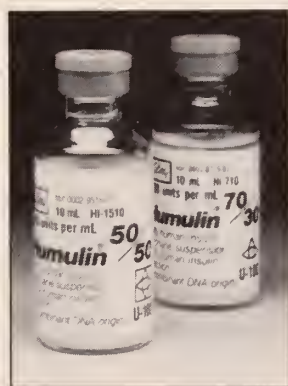
- 71 **Sessions; Officers, Councilors, and Trustees; Members; Nominating and Reference Committees; Report of the House Committee on Bylaws**
- 10A MEDICAL MEETINGS AND LECTURES



Because One Size Doesn't Fit All...

New Humulin 50/50 is the tailor-made answer to individual patient needs. A unique combination of equal amounts of Regular human insulin and NPH human insulin, it will be useful in situations in which a greater initial insulin response is desirable for greater glycemic control.

Like Humulin 70/30*, new Humulin 50/50 offers the convenience and accuracy of a premix. And it can be used in conjunction with an existing 70/30 regimen.



New **Humulin** ⁵⁰/₅₀

50% human insulin
isophane suspension
50% human insulin injection
(recombinant DNA origin)

The Newest Option in Insulin Therapy

WARNING: Any change of insulin should be made cautiously and only under medical supervision.

* Humulin® 70/30 (70% human insulin isophane suspension, 30% human insulin injection [recombinant DNA origin]).



Global Excellence in Diabetes Care

Eli Lilly and Company
Indianapolis, Indiana
46285

AIM HIGH

BE AN AIR FORCE PHYSICIAN.

Become the dedicated physician you want to be while serving your country in today's Air Force. Discover the tremendous benefits of Air Force medicine. Talk to an Air Force medical program manager about the quality lifestyle, quality practice and 30 days of vacation with pay per year that are part of a medical career with the Air Force. Find out what it takes to qualify. Call

USAF HEALTH PROFESSIONS
TOLL FREE
1-800-423-USAF



"I'm practicing medicine the way I think it should be practiced, sans the paperwork and administrative overload."

Owen Brodie, MD, joined CompHealth's locum tenens medical staff in 1989, after 21 years in private practice. Since

then he's worked in temporary assignments in state facilities, filled in for attending physicians, covered for private practitioners across the country.

A pilot. A historian. A board-certified psychiatrist. Southern to a fault. Owen Brodie knows...

It's a great way to
practice medicine

CompHealth
L O C U M T E N E N S

1-800-453-3030

Salt Lake City ■ Atlanta ■ Grand Rapids, Mich.

WANT DISCOUNTS ON YOUR EXISTING INSURANCE?

We provide complimentary 2nd opinions on your disability and life insurance to provide you with the lowest rates. Servicing physicians exclusively. *References provided upon request.*

Paul R. Sheinkopf
Sheinkopf & Associates
EAB Plaza West, 5th floor
Uniondale, NY 11556-0137

516-357-8700

FAX 516-357-8891

PRACTICE OPPORTUNITIES

FAMILY PRACTICE:	Upstate New York, Illinois, Wisconsin, Michigan and Arizona
INTERNAL MEDICINE:	Wisconsin, Illinois, Minnesota, Arizona and California.
NEUROLOGY:	Upstate New York.
OB/GYN:	Upstate and Long Island New York, Ohio, Illinois and Arizona.
ORTHO SURGERY:	Upstate New York, Illinois, Wisconsin and Arizona.
PEDIATRICS:	Ohio, Michigan and Wisconsin.
PM & R:	Wisconsin
PSYCHIATRY:	Ohio

All inquiries are confidential. For additional information call:

GIELOW ASSOCIATES, INC.
1-800-969-7715

SELLING YOUR PRACTICE? NEED A BUYER NOW?

Countrywide can provide you with the largest network of qualified buyers and a transaction to secure the best possible price and terms for your practice. Countrywide has helped hundreds of your colleagues buy and sell their practices. To learn how we can do the same for you, call us today at (800) 222-7848.

Countrywide Business Brokerage, Inc.
319 East 24th Street, Suite 23-G
New York, NY 10010

Classified Advertising

PHYSICIANS WANTED

NATIONWIDE TRAVEL—Health research organization seeks physician for National Health & Nutrition Examination Survey sponsored by the U.S. Public Health Service. Individual will be part of a large medical team conducting health examinations in govt. mobile exam centers traveling to 88 areas of the U.S. through Fall of 1994. Must be licensed in one state. One year minimum commitment and Full-Time Continuous Travel Required. Competitive salary, paid malpractice, per diem, car, four weeks paid vacation per year, holidays, and health, life, dental, disability insurance offered. Call Beverly Geline, 800-937-8281, ext. 8248. Westat, Inc., Rockville, Maryland. EOE/M/F/V/H.

New York State Journal of Medicine



COMMENTARIES

Health challenges for the 1990s

Arriving back in the state of my birth—the state where my father and grandfather have practiced medicine for two generations—I assume the position of New York State Health Commissioner at a time of great challenge and possibility. The Chinese language character for the term “crisis” comes to mind. It is made up of two signs: one for “danger,” and one for “opportunity.”

That describes our situation here in New York at the beginning of the final decade of the century.

I want to share some of my perspectives on major problems in health care confronting us in New York State and discuss priorities that I see for the department, health care reform, and the challenges that lie ahead.

My career has given me the opportunity to view the American health care system from a number of different perspectives. I have practiced medicine on the front lines of the emergency department. I have been an administrator for the Medicare program. I have been a researcher, and I have seen the health care system from the vantage point of American business, which faces continuing, staggering cost increases and is not persuaded the health benefits are worth the costs. Nor, frankly, are all members of the public so persuaded.

PUBLIC HEALTH THREATS

First, the dangers. They are not in short supply. Foremost among these are the public health epidemics of human immunodeficiency virus (HIV) and acquired immunodeficiency syndromes (AIDS), tuberculosis (TB), measles, and syphilis. These diseases have stretched our neglected public health infrastructure nearly to the breaking point. They severely tax our ability to reach our neediest citizens, and they present us with unprecedented ethical and moral dilemmas. These epidemics occur in the context of broad social problems: high teen pregnancy rates, poor nutrition, drug abuse, and homelessness. In addition to these enormous burdens, New York State is also in the midst of the most severe rabies epizootic in our history. Nor are these the only significant public health problems with which we need to deal. Breast cancer, tobacco addiction, and the manifold environmental threats to health are some of the most

important priority areas. To make the challenge even greater, we must fight the epidemics and other public health problems with shrinking resources. Let me highlight just two of these, HIV and TB.

HIV AND AIDS

New York continues to bear a terrible and disproportionate share of the AIDS burden; 22% of the nations AIDS patients are New Yorkers, and a remarkable 31% of US women with AIDS are New Yorkers. HIV, being the extraordinary phenomenon that it is, requires extraordinary solutions.

For example, in the first month of my tenure, we reviewed grant proposals for needle exchange (not give-aways) and found four in New York City that were fundable from the standpoint of science and good public health policy. These are programs that can get contaminated needles off the street, in addition to placing clean needles in the hands of those who use intravenous drugs. We will continue to evaluate those proposals and fund the ones that are scientifically sound, that provide secure service as part of an overall HIV and drug education project, and that give the department a chance to evaluate their impact.

Second, we have to recognize that explicit sex education is a critical part of fighting this epidemic, even though we (those of us with teenage children or siblings, anyway) would probably select abstinence as the preferred method of avoiding the virus. Yes, abstinence is the best. However, there is a large segment of our young population that is not abstinent, and we have a duty to protect them as well. So I publicly support the position of the chancellor of the Board of Education in New York City, not to restrict the public health efforts of AIDS educators in the schools, and I must endorse explicit education and even condom distribution, as well, where and when local communities agree.

TUBERCULOSIS

We in medicine thought we had tuberculosis licked. We were wrong. I spent four months of my internal medicine residency on a chest service that housed the

only in-patient TB ward in Los Angeles County. I saw tuberculous arthritis, meningitis, peritonitis—all sorts of complications that most physicians growing up in this era have not seen. I thought I had a window on a medical museum that would not be directly relevant to the rest of my career. That turned out to be quite a wrong perception. In New York State in 1991, we had 4,500 cases of tuberculosis; in 1978, the number was 2,100. The rate of tuberculosis in New York State is 23 per 100,000, more than double the national rate in 1991.

Yes, the tuberculosis epidemic is certainly related to HIV and drug abuse. However, the pattern of tuberculosis incidence in this country over the century looks like a straight line going down until about the early 1980s. Most of that decline occurred before any effective treatment for TB was available. The decline occurred because we paid attention to socioeconomic conditions and sanitation, public health, housing, and food needs. The resurgence in tuberculosis is not a medical issue alone. In many of our communities, we are recreating the circumstances of overcrowded, substandard housing, poverty, and poor nutrition that led to the spread of tuberculosis in the earlier part of this century. To confront these traditional enemies, we have a public health infrastructure that has decayed to the point of impotence; mobile x-ray vans are gone, the public health chest clinics are nearly gone, hospital isolation beds are gone, and the core of public health nurses is barely functional. Clearly, the challenge is not only in medicine and in public health, but also social, economic, and political.

ACCESS TO HEALTH CARE

We must look beyond the immediate manifestations of the epidemics to their basic causes to understand how to prevent similar threats in the future. So, although I would identify the epidemics as the most immediate threat to our state's health, I believe lack of access to basic health care is the crucial underlying problem.

As a society, we will be judged harshly if we fail again in the 1990s to provide necessary and effective health care, with no discrimination and no rationing, to all our citizens. An estimated 35–38 million people are uninsured in this country. In New York State, the number is 2.1 million, or 12%, in 1991, a trifle under the national average of 14%.

Some interesting facts about the uninsured population in New York State:

- 80% of the uninsured population in New York State are employed or are dependents of employed persons;
- half work in small business;
- 20% are children—421,000 children without insurance;
- 30,000 pregnant women a year are without insurance.

The public health implications of those numbers are truly shameful. We are unable to provide necessary and effective care to all of our citizens. The United States and South Africa are the only industrialized nations that have failed to provide universal health care to citizens. How did we let this happen in a country founded on egalitarian principles, on caring, and on community?

The problem of access is not just a problem of insurance. Many insured people do not have access to continuous sources of primary care, a major part of the

problem of access. Both in the nation and in the state, there is a major imbalance between specialty care and primary care. Seventy percent of practicing physicians are specialists, and only 30% are primary care physicians. Those percentages exactly mirror the distribution of training slots in the state—70% are specialty slots, and 30% are primary care slots. The fact that 80% of physicians practicing in New York State are trained here makes it clear that the phenomenon is self-perpetuating and cannot be properly redressed until our great specialty training centers shift the balance between specialty and primary care training.

The State Council on Graduate Medical Education (GME) has made some extraordinary progress in dealing with this issue in recent years, and we look forward to pursuing a number of its suggested reforms in this area, including creating additional financial incentives to attract physicians into, and keep them in, primary care. We have already modified the indirect GME formulas at the state level to reward primary programs.

OPPORTUNITIES

Opportunity abounds if we are brave enough to grasp it. As with the GME issue I discussed above, there are plenty of opportunities available for progress. I am convinced that the public and professional debate about the future of American health care has risen to the point that will provide ample openings for us to design realistic and thorough-going solutions to our problems. These will not come easily, but they are possible. Let me explain.

COST CONTROL

What has been impeding a solution to the problem of access? I think the main impediment is cost. We will not achieve consensus on a way to improve access until and unless the ever increasing spiral of cost increases is stopped. All payers are affected by this problem. The state budget is thrown out of whack every year, increasingly so by the Medicaid budget; the federal budget is thrown out of whack by the increasing demands on the Medicare Trust Fund; and private payers—employers, private health insurance companies—continue to see increases of 20%, 30%, and 40% in the premiums they pay for health insurance.

I think the cost problem has three components: overuse, efficiency, and new medicine. We can have a salutary impact on the problem if we're serious about it. That means attacking the tough underlying problems—not simply the easy rhetorical targets like administrative red tape and malpractice lawyers.

Overuse. Our first responsibility is to attack the problem of overuse because that will allow us to improve quality and to control costs at the same time. With all the overuse in the system, it is irresponsible to propose explicit rationing—that is, to say formally that we will not provide necessary and effective care under some circumstances, simply because we cannot afford it. It has been conservatively estimated that 20% of what we do in clinical medicine is not necessary. That's where our principal cost containment efforts ought to be focused.

Efficiency. This is another area. We can define that as producing the same things we do now but with a lower use of resources at less cost. There has been some progress on this score, but not enough. We have failed to bring physicians into the process of making hospital care more efficient, and I believe that is from where further gains will come, from physicians looking at their own practices and starting to compare them with practices in other institutions. It is very unusual, for example, for a group of surgeons from the Northeast to sit down with a group from the West and ask "Why is the postoperative length of stay for a laminectomy longer in New York than in Los Angeles?" "What are we doing differently?" "Can we get some agreement on what optimal practices ought to be?"

I think the State Health Department can be a facilitator: not a dictator, a facilitator providing data and making clinical exchanges easier. So that is the second component, efficiency, and we have got a long way to go before we conclude that we cannot make health care more efficient.

New Medicine Technology. The third major contributor to health care costs—new procedures, new technologies, new drugs, new treatments, new diagnostic tests—will defeat us, even if we are able to solve the other two components. We must arrive at a balanced situation in which, without discouraging innovation, we evaluate new tests and treatments and use them appropriately.

Consider computed tomography scans of the cranium. That technique absolutely revolutionized the treatment of patients with head trauma and improved their quality of care. We got enthusiastic about these machines and produced them in huge numbers. They did get used for people with head trauma, fortunately. However, they also got used for people with headaches, dizziness, confusion, and a whole range of other problems where no benefit has been demonstrated. In fact, in many circumstances the benefit is practically nil or negative. Lithotripsy, PTCA, and magnetic resonance imaging have had similar patterns. Until we get a handle on that problem, it will be extremely difficult to deal seriously with health care costs.

Certainly physicians and health care institutions have a large part to play in the process of gaining control of all parts of this cost spiral, but like tuberculosis, this is not a medical problem alone. This is a broader social issue.

I was on a panel recently with Dr Robert Waller, president of the Mayo Clinic, and he remarked: "The problem is not with technology. It is we who use it that are the problem." Well, yes, in part. It is true that those of us who are trained to use high technology machines tend to like to use them, just as a pilot likes to fly. We like to use the skills we have honed. However, physicians are not flying solo, if I may continue the analogy. We are part of an activist culture. We Americans like action. The media tells the public all about the wonderful new machines and cures and technologies, and patients tend to expect they will get the benefit of them. Patients do not like to go away with a prescription to "do nothing."

So, although I agree with Dr Waller's dictum, "Physician, control thyself," one has to recognize the physician responds to a variety of forces and stimuli.

QUALITY OF CARE

I have discussed public health issues, cost, and access. Another area of concern and priority for us is quality of care. A growing body of research documents that in fact we have some serious quality problems in American medicine.

There are three kinds of quality problems: overuse, underuse, and misuse. I have discussed underuse, which is another way of saying access. I talked about overuse, and I think that needs to be a major focus for us because of the quality and cost implications. That leaves misuse, where so much energy is spent.

The government, the medical profession, and even hospitals have tended to use quality control as a punitive mechanism, defining mistakes that individuals have made to find opportunities to blame people and then use the quality assurance system as the means to punish nurses, hospitals, and nursing homes who cannot or will not improve the quality of care they provide. However, the punitive option ought to be the one of last resort in my view. I think that the best way to improve quality is by getting those who are delivering the care to galvanize and pursue the process of quality improvement.

What I hope to do is move away from quality improvement as a punitive process, away from depending on external regulation, external controls, and inspections, to an internal process resulting in a collaborative relationship with the Health Department. The department's role should be that which we can do best—that is, to collect data and feed it back to hospitals. Hospitals and physicians now can look at their own practices, but they do not have much of an idea where they stand with respect to their peers. We can provide that information and also facilitate the sharing of best practices. For example, we have a state of the art data set on the outcomes from cardiac surgery. It is better than any research data set in the nation. What we do not yet have is a good understanding of what produces the enormous variability in risk-adjusted mortality among hospitals. We need to understand it.

The Health Department ought to be helping institutions to look at each other's processes of care, so that we can start to understand what is producing these very different outcomes again, with the goal being not to punish but to share best practices among institutions so that everybody's quality is improved. We have begun to do that with nursing homes in some areas of the state, and in Syracuse, the industry has formed an advisory committee to facilitate this promising process.

One of the most promising avenues for dealing effectively with all three types of quality problems is the rapidly developing field of practice guidelines. I believe they represent a practical way for us to specify how to deal with a particular clinical problem. They also become the template against which we measure how well we are actually doing. That comparison then becomes the basis for specific quality improvement actions.

One of the early goals that I have set for the department and for myself personally is to diminish the adversarial nature of the relationship between the department and hospitals, nursing homes, physicians, and other health care practitioners. The issues are too big,

the resources are too scarce, for us to burn them up in the friction that results from the kinds of adversarial confrontations that have sometimes characterized those relationships in the past.

HEALTH CARE REFORM

Finally, I would like to comment on the matter of health care reform. I am a strong advocate of health care reform, by which I mean creating a system that provides universal access to quality health care for all citizens, at an affordable cost.

I am heartened by the widespread discussions and debate on this topic, but I am not so sanguine to think that the new President has a magic wand in his hand and the promised land is just around the corner. The promised land has been "just around the corner" for a good 20 years, it seems to me. Sometimes I think we must be going around a circular building: the corner never appears. In addition, although there has been a lot of discussion on the topic, the discussion has not really focused on the tough issues.

Designing a system to reform our health system must start with three basic goals: universal access, assured quality, and affordable costs. I have discussed all three in the context of New York State. Solving any two of those problems at once is not so difficult. You can have universal access and top quality if you do not care about the costs. You can have access and a limit on costs if you do not care about the quality. The trick is to achieve all three, and virtually all of the national plans I have seen do not meet this test, or even try. So, while I believe that

the new Clinton administration will seriously undertake some form of national health reform, I also expect that a lot of the real work will be left to the states. I expect that the new administration will offer the states broad flexibility to design their own systems.

Here in New York, this represents a positive challenge. We are already well underway designing and even implementing pilot programs that will provide us with the tools to deal with universal health care reform. We need to keep moving in areas where we already know we can make a difference.

- We have a single payor demonstration program that helps 20-odd hospitals collect their bills faster and more easily, through an electronic claims clearing house. Physicians are being invited to join now, too.
- We have a Child Health Insurance Program that provides low costs, subsidized insurance to up to 50,000 children under age 13. The program is so popular that we have waiting lists.
- We have enhanced Medicaid rates for primary care physicians who provide a package of basic services to children.
- In addition, we appear to have a commitment from all the major players in the field, to work toward a consensus reform program. The Medical Society, the hospitals, the insurance companies, the labor unions, and the business community are all actively involved and participating in our Health Reform Task Force, which is designed to move us from debate to real change.

The challenges are great and so are the opportunities.

MARK R. CHASSIN, MD, MPH

Commissioner of Health

New York State Department of Health

Corning Tower, Room 1455

Albany, NY 12237

Cost containment and academic medicine

For more than two decades, the word "crisis" has been used in nearly every discussion of medicine and health care in the United States. For most of this period, however, various surveys indicated that Americans, by and large, were satisfied with their personal medical care. Furthermore, since fairly standardized health benefits covered the needs of a majority of people during normal employment periods and before the sharp inflation of health care costs, issues of cost were not a widespread preoccupation with the average citizen. Thus, the perceived "crisis" was more figurative than real.

By the end of the 1980s, attitudes changed profoundly. Among the problems that currently beset the American health care system, three are particularly nettlesome.

1. Lack of appropriate access to affordable care, especially primary care services, for perhaps as many as 50 million Americans.
2. Escalating costs of hospital and physician's services.
3. A perception of inconsistent levels of quality in medical care.

Report and recommendations of the Associated Medical Schools of New York, Committee on Cost Containment. Jordan J. Cohen, MD, Chairman.

Address correspondence to Mr Frank Jones, Executive Director, Associated Medical Schools of New York, 70 West 36 St, Suite 302, New York, NY 10018.

Few disagree that academic medicine must provide leadership in addressing these problems. However, in responding to societal concerns, medical schools must not lose sight of their essential mission of providing high-quality education and maintaining an abiding commitment to research.

In a 1991 paper, "Primary care in New York State," published in the *Journal*, the Associated Medical Schools (AMS) of New York expressed its position on access to care, the first of the three national problems noted above.¹ The present communication focuses on the second, excessive cost, which was the topic of the 1991 AMS Retreat.

Several experts made presentations during the Retreat, emphasizing the complexity of the cost problem and the elusiveness of solutions. During these discussions, the following factors in escalating costs were noted:

- The aging of the population with accompanying complex problems and increased need for care.
- Proliferation in the use of effective but costly technologies. Inappropriate use of such technologies is a related and important consideration.
- Mounting epidemics (ie, AIDS, substance abuse, tuberculosis, alcoholism, and trauma).

- Reliance on high-cost hospital emergency rooms for the delivery of primary care in the inner city.
- Geographical maldistribution and specialty imbalance (ie, too many specialists, too few generalist physicians).
- Increased costs for medications.
- Increases in administrative costs and the cost of complying with regulations.
- Unnecessary procedures resulting from "defensive medicine."
- The high cost of professional liability insurance.

In the face of such forces, many of them difficult to control, how can our society contain health care costs? In attempting to find answers, one must not lose sight of medicine's unique characteristic: Its central involvement in health and illness, life, and death. At some point, nearly everyone confronts serious illness, often life-threatening. In those moments, cost containment is furthest from the central concerns of the patient and his or her family, and no health policy or regulation will ever alter that fact. Whether society can ever be able to allocate adequate resources to satisfy patients' legitimate desires and needs in such circumstances, the ability of physicians to respond to them is a central issue in the health care cost problem.

This caveat notwithstanding, many factors escalating costs are controllable, and the responsibility for cost containment must be shared by many sectors in society, including academic medicine. Decisions made by physicians account for a major portion of medical care costs. Their attitudes and approaches to medical practice are shaped to a great extent during medical school and graduate training.

The challenge to medical schools therefore is to instill in future physicians the traditional dedication to quality along with an awareness of the cost implications of their actions and decisions.

Where to begin? As a fundamental guiding principle, medical education must re-affirm that the practice of high-quality medicine includes sensitivity to its cost. If we teach this principle, we must also practice it.

Medical schools can exert their influence through their twin missions of education and research and as standard setters of quality in patient care. The initial focus should be on graduate medical education. Residents are among the primary teachers for medical students in their clinical years. Thus, residents must first understand and appreciate the importance of the cost implications of their clinical decisions and of the diagnostic and therapeutic procedures they prescribe. They must be aware of the rapidly changing practice environment in which they themselves will work, an environment in which cost containment will be a pervasive factor. A major contributor to this environment is the expansion of managed care in its various configurations. Government policy makers and corporations are clearly convinced that managed care offers an important and potentially effective mechanism for achieving cost control. This view is by no means unanimous among cost experts, and many continue to have concerns about the quality of care provided in HMOs and similar organizations. Nevertheless, given the clear directions of government, third-party payers, and corporations, reimbursement will increasingly be structured to encourage the provision of care in these modalities, and future physi-

cians should be trained for service in such practice environments.

For medical students, one step that might have an impact on attitudes and practice philosophy would be to supplement the curricular attention currently given to the care of individual patients with comparable attention, both didactic and experiential, to the health needs of communities. There is ample evidence confirming the impact of societal, environmental, and behavioral influences on personal health. Concerns about cost therefore give added importance to efforts to change risky personal habits and promote healthful behavior among individual patients and in the community at large. This approach, which can be encouraged by the medical schools, clearly will not yield a quick payoff, but it could make the most significant difference in demand for care and in cost over the long run.

While considering curricular innovations, we should not overlook the importance of re-emphasizing fundamentals by insisting that diagnostic evaluation and treatments be guided by careful recording of a patient's history and performance of complete, thorough physical examinations. Students must be better taught how to use the basic information obtained through these bedside skills to minimize the need for expensive diagnostic tests.

Inherent in these suggestions is the need to heighten physicians' awareness of decision analysis, enhance the teaching of clinical epidemiology, and raise the academic structure of such traditional subjects as preventive medicine.

The traditional research mission of academic medicine can also be turned into a powerful tool to address issues of cost. Medical schools should take the lead in developing guidelines for appropriate use of high cost technology. Studies have indicated that as much as 30% of technology use is inappropriate. The need for a careful assessment of the benefits of new technology is obvious.

Discussions at the Deans' Retreat also touched on a much thornier issue for academic medicine: physician supply. This issue was the subject of intense debate more than a decade ago with the publication of the Graduate Medical Education National Advisory Committee report. That report foresaw a physician surplus at the close of the 20th century, particularly in the highly specialized fields of medicine. Since increased numbers of specialists tend to increase costs and since access to care is more closely related to geographic and specialty distribution than to the absolute number of physicians, academic medicine must find ways to address the issue of appropriate physician supply.

Recognizing the importance of this issue, the New York State Department of Health established the Council on Graduate Medical Education in 1987 with the goal of reducing residency positions in the State by about 30%. This aim became unrealistic with the revisions to part 405 of the State hospital regulations, reducing the hours worked by residents. In spite of the view of academic medicine that graduate medical education should be focused on education and not be driven solely by service needs, the fact remains that house staff are

generally the mainstay of medical care in teaching hospitals and are seen as the first line of defense in the battle against AIDS and the many other major and complex illnesses that have become part of the urban health care crisis. If these residency positions are significantly reduced, other types of care-givers will be needed to provide the services, such as nurse practitioners and physicians' assistants. These care-givers are already in short supply, and their use will mean potentially higher costs.

Few studies of access to medical care and of cost containment yield genuinely new ideas, and many frequently conclude that there is no money to implement the old ideas, whatever their merit. Moreover, the argument that we need to spend more money to reduce costs is certain to engender some skepticism. Nevertheless, that is the reality. Curricular innovation, expanded training at non-hospital-based ambulatory sites, improved reimbursement for primary care, expanded health services research, and technology assessment are all costly, yet without them, the cost of health care is not likely to be controlled. Private philanthropy can provide some seed money, but the bulk of financial support for these educational initiatives must come from government and other third party payers. As always, the likelihood of such support depends on government priorities and the degree to which there is agreement that these investments will ultimately lead to improved access and cost-effective care.

There is broad agreement that one important step in halting the escalating cost of care is to increase the availability of primary care services, particularly in the inner cities where people depend on high-cost emergency rooms rather than physicians' offices for their basic medical care. The position paper on primary care prepared by AMS in 1991 provides a backdrop for these recommendations on cost containment.¹ The primary care paper articulated the commitment of the State's 13 medical school Deans to enhancing the stature of primary care training, respecting, at the same time, their differing institutional missions. In beginning the implementation of these recommendations, the AMS Committee on Primary Care developed a concept for a fellowship program aimed at expanding faculty role models in primary care. In addition, virtually all New York medical schools are seeking philanthropic support for initiatives in primary care education, and nine of the 13 schools now have departments of family practice.

The primary care paper also encouraged development of a partnership among the various organizations and constituencies in the State to develop collectively a plan for enhancing access to care among underserved New Yorkers. AMS reiterates its commitment to that priority, with the added agenda item of cost containment.

The basis of such a partnership has already been formed. Representatives of the New York medical schools have been involved in discussions with the New York State Department of Health, the State Council on Health Care Financing and the State Council on GME regarding ways to enhance primary care. These discussions should be expanded to include cost containment.

Many entities in New York are looking at these issues from a variety of perspectives, and many have overlapping concerns. To bring these diverse entities together, a gubernatorial task force could offer an effective forum. We urge the Governor to establish a task force to include representatives of State Government, the State Council on Graduate Medical Education, New York City's health leadership, AMS, hospital associations, the Medical Society of the State of New York, major third party payers, and other appropriate constituencies. The focus would be on the linked priorities of access to care and cost containment.

In summary, AMS offers the following recommendations:

- Medical school faculty should be encouraged to re-affirm, both in their teaching and by example, the basic principle that good medical practice embraces cost effectiveness.
- Graduate medical education should provide opportunities for residents to gain a specific understanding of the cost implications of their clinical decisions and of the prominence that cost considerations will be given in the future practice environment.
- Medical schools should broaden their curriculum where necessary to increase emphasis on population medicine, paying increased attention to prevention and to the physician's role as a change agent for health in his or her community. Specific attention should also be paid to strengthening decision analysis and clinical epidemiology.
- AMS should study the feasibility of a consortium-wide technology assessment effort.
- AMS will maintain its current dialogue with the State Departments of Health and Education, the Council on Health Care Financing and the State Council on GME, and will intensify its interaction with legislative leaders and the Governor's office to encourage a collective solution to the problems of access and of the escalating cost of health care.
- AMS and its member schools will intensify efforts to sensitize medical students and residents to their social responsibility to care for patients of all socioeconomic and cultural backgrounds and to enhance their ability to do so effectively.

JORDAN J. COHEN, MD

JULES COHEN, MD

ALBERT S. KUPERMAN, MD

ANTHONY P. TARTAGLIA, MD

FRANK JONES

Associated Medical Schools of New York

70 West 36th St, Suite 302

New York, NY 10018

1. Finberg L, Adler K, Cohen J, et al: Primary care in New York State: Report and recommendations of the Associated Medical Schools of New York. *NY State J Med* 1991; 91:450-453.

The status of the *New York State Journal of Medicine*: Where are we?

At the upcoming annual House of Delegates meeting in March, delegates may be asked to choose between continuing the *New York State Journal of Medicine* as a peer-reviewed clinical and scientific journal or replacing it with a socio-economic tabloid. The Committee on Publications, Library, and Archives (Publications Committee), which is formally and officially charged by the Medical Society with overseeing the *Journal*, strongly opposes the proposal to replace the current scientific and clinical publication with a socio-economic tabloid.

EXCELLENCE OF THE NEW YORK STATE JOURNAL OF MEDICINE AS A CLINICAL AND SCIENTIFIC PUBLICATION

The *Journal* is one of the premier peer-reviewed clinical and scientific medical publications in the world. The following facts provide some idea of the *Journal's* excellence.

- Ranked in the top 12% of the 2,400 medical journals indexed by the *Index Medicus* in terms of its impact on medical science.
- Among the top 5% of peer-reviewed medical journals whose content is considered crucial to medicine and which is rapidly indexed each month by the National Library of Medicine.
- Chosen in 1992 by the Library of Congress as a publication of excellence.
- One of 400 medical journals out of a world total of 5,000 that adheres to the requirements of the International Committee of Medical Journal Editors.
- Receives several hundred requests a year from other journals and book publishers to reproduce the materials from published *Journal* articles.

There are some 5,000 medical journals published in the world, 2,600 of which are "throw-aways" whose content is considered too unreliable to be considered for indexing by the National Library of Medicine. In addition, there are numerous medical newspapers and tabloids covering socio-economic issues whose content is not indexed by the National Library of Medicine and which are not even retained in library collections. The *Journal's* ranking as assessed by outside groups such as the National Library of Medicine and the Library of Congress characterize it as a publication of excellence.

WHAT THE MEMBERS AND READERS WANT

We, the members of your Publications Committee, are aware that the opinions of our members and readers are as important as the evaluations of national standard-setting bodies. Therefore, in late 1987, the Committee authorized a comprehensive readership survey for the *Journal*. This survey of a random sample of 1,550 readers was conducted by Health Industries Research, a Connecticut-based company recommended by Donald F. Foy, the Society's Executive Vice-President. He concurred with the Committee that a disinterested and experi-

enced survey company was required to design, implement, and analyze the survey for it to have credibility. The important results of that survey revealed the following:

- 47.5% of those surveyed responded, a high return rate providing reliable information.
- 78%, a clear majority, rated the *Journal* as good or excellent.
- 84%, a clear majority, rated the peer-reviewed clinical-scientific format as good or excellent.
- 60% of respondents spent 20 minutes or more reading each issue of the *Journal*; 33% of respondents spent more than 30 minutes reading the *Journal*.
- 85% of respondents read all/most or selectively read commentaries.
- 81% of respondents read all/most or selectively read research papers.
- 80% of respondents read all/most or selectively read case reports.
- 76% of respondents read all/most or selectively read the clinical conferences.

The results of this readership survey clearly showed that the vast majority of members and readers were highly satisfied with the peer-reviewed clinical and scientific editorial content of the *Journal*. Not a single respondent suggested that the *Journal* be transformed into a socio-economic tabloid.

THE COSTS OF PRODUCING THE JOURNAL

Given the Society's financial problems, the Publications Committee has responsibly made regular economies in the costs of producing the *Journal*. In 1982, \$721,329 were spent on the *Journal*. In 1991, only \$511,854 were spent on the *Journal*, representing a 30% reduction over nine years, a period of time when production costs were rising by 3%–4% per year. The total costs outlined above also include the operation of the library, which serves the membership, and the running of the Information Services, which provides help to some 20–30 non-physician callers per day. In 1991, the library handled 684 bibliographic and reference searches for society members, and 1,970 telephone inquiries from members. A total of 1,718 items were requested on interlibrary loan, and 3,392 books and journals were circulated.

THE JOURNAL'S FINANCIAL PROFIT

The *Journal* has three major sources of income—advertising revenues, income from reprints and subscriptions, and that portion of the dues that members are regularly told go for a subscription to the *Journal*.

Until 1992, this notice read: "\$30 of your dues goes for a subscription to the *New York State Journal of Medicine*." The 1993 dues renewal notice no longer carries this statement. However, a similar statement, "The annual subscription rate for members (\$30) is

included in the annual membership dues," now appears on the *Journal's* masthead at the request of the Executive Vice-President.

In 1991, the *Journal's* income was as follows:

Advertising.....	\$243,437
Reprints and subscriptions.....	32,447
\$30 dues allocation	513,370
TOTAL	\$789,254

The *Journal's* profit for 1991 was \$175,991, after allowing for indirect costs, such as heat and light.

THE ARGUMENT OF THOSE WHO CLAIM THAT THE *JOURNAL* RUNS AT A FINANCIAL LOSS

Some of those who are advancing the cause of transforming the *Journal* into a socio-economic tabloid have consistently claimed that the *Journal* runs at a financial loss. However, in making this argument, they refrain from telling listeners that they exclude as income the \$30 of annual dues each member is told goes for the *Journal*. When challenged on this, they claim that the \$30 of each member's dues should not be counted as *Journal* income, in spite of the fact that members are told that this amount goes to the *Journal*.

They say that the statement appears to satisfy the US Post Office and Internal Revenue requirements, and that therefore the Society is not bound to allocate it to the *Journal* and can use it for other purposes. Thus, over the years, the \$30 of dues that members have been told go for the *Journal* have not, in fact, been allocated in full to the *Journal*.

We the members of your Publications Committee have repeatedly reminded them that the \$30 statement represents a moral and legal contract with the membership.

In October 1992, the executive administration of the Society, which had not viewed the \$30 dues amount as a sum dedicated to the *Journal*, requested that the following statement be added to the masthead: "The annual subscription for members (\$30) is included in the annual membership dues." This reflected, if only indirectly, a shift in position and a recognition that the \$30 of dues are indeed legitimate *Journal* income.

INITIAL ATTEMPTS TO DISCONTINUE THE *JOURNAL* AS A PEER-REVIEWED CLINICAL AND SCIENTIFIC PUBLICATION

The past year has witnessed an intensification of efforts on the part of some to replace the *Journal* with a socio-economic tabloid. However, these efforts began well before this. In 1986, the Executive Vice-President of the Society made it very clear to your Publications Committee and to the editorial staff of the *Journal* that he did not support the Society's publication of a peer-reviewed clinical and scientific publication. At meetings with us, he promoted the transformation of the *Journal* into a socio-economic publication and presented specific examples of what he thought we should emulate. His non-support of the *Journal* as a peer-reviewed clinical and scientific publication has been both consistent and intensified in character, reflecting, in our view, a philosophical commitment to removing the Society from clinical and scientific activities.

In 1990, the Executive Vice-President entered into discussions with several mid-Western state medical journals and one county medical society bulletin to pursue the establishment of a joint socio-economic *Great Lakes Medical Journal*. None of the publications in question are peer-reviewed. These discussions took place without your Publications Committee's knowledge. In August 1991, after the Great Lakes proposal proved a failure, the Executive Vice-President initiated discussions with Chase Communications, the publishers of *New York Doctor*, a throw-away, which proposed taking over the publication of the *Journal*. These discussions took place without any involvement of the Publications Committee.

THE MEMBER NEEDS SURVEY OF 1991

In 1991, the Society contracted with a survey firm to undertake a Member Needs Survey. Since your Publications Committee was planning a new readership survey, we specifically requested that no questions about the *Journal* be included in the Member Needs Survey. This request of ours was based on the fact that survey companies informed us that inclusion of questions about the *Journal* might reduce the response rate to our subsequent readership survey. In spite of this request, two questions about the *Journal* were included in the Member Needs Survey. When the results of the Society's Member Needs Survey were published in October 1991, your Publications Committee was deeply troubled by the following flaws in it:

- A response rate of only 28.24%, making the information highly unreliable.
- Defects in question design.
- The sandwiching of questions about the *Journal* in between those about health care regulation which regularly elicit strong negative responses.
- The carry-over effect of strong negative responses about government regulation to other questions, including those about the *Journal*.
- Strong negative responses about many Society benefits and services, confirming that the respondents represented a highly biased group of disaffected individuals.
- Even when the *Journal* was rated highly, such responses were editorially characterized as "low."

WHAT IS A VALID SURVEY RESPONSE LEVEL?

We are planning a new readership survey. In preparation for this, we sent out a Request For Proposals (RFP) to several survey companies. At the same time, we contacted several eminent epidemiologists, biostatisticians, and the Director of the National Center for Health Statistics to ascertain the level of response required for a valid survey. We were advised by highly respected authorities at City University, Columbia University School of Public Health, the University of Kansas School of Medicine, and Tulane University that an overall response rate below 30% would be biased and invalid, and that no conclusions could be drawn from it. The Director of the National Center for Health Statistics informed us that he and his colleagues would have very serious concerns about a survey response rate less than 30% and that potential errors in such a low response rate would be high.

The survey companies, which we determined to be the most experienced for conducting a readership survey

told us that they would not accept less than a 45% response rate to any survey.

In view of these expert opinions, we conclude that the low response rate of 28.24% achieved in the Member Needs Survey produced results which are unreliable.

THE AD HOC TASK FORCE ON PUBLICATIONS AND COMMUNICATIONS

Once the results of the Member Needs Survey were available, the Council of the Society appointed an Ad Hoc Task Force on Publications and Communications. The charge of this task force was to study the Society's publications and communications. In January 1992, we the members of your Publications Committee undertook two initiatives to assist the task force. We instructed the *Journal* editor to offer assistance and information to the chairman of the task force, and we did the same.

REFUSAL OF THE CHAIRMAN OF THE AD HOC TASK FORCE TO ACCEPT ASSISTANCE, ADVICE, AND VIEWS FROM THE PUBLICATIONS COMMITTEE

On January 23, 1992, the *Journal* editor contacted the chairman of the task force and offered to be of assistance. The chairman told the editor of the *Journal* that he and the task force needed no information or input from him. In addition, he told the editor that nothing would prevent the task force from achieving its objectives of radically changing how the Society communicated with its members.

The same day that the editor initiated his offer of assistance to the task force, we the members of the Publications Committee did likewise. Although the chairman of the task force responded to us in a letter of January 27, 1992, he did not invite us to appear before the task force and did not accept our offer of providing help and information. Instead, he told us that the charge to the task force was drawn from the Member Needs Survey, which so many consider biased and invalid.

On March 4, 1992, we sent a second letter, offering assistance by virtue of our experience with the *Journal*. In it, we said: "We would once again like to express our willingness to cooperate with the task force and to be of assistance to it. We would like to make a presentation to the task force at its meeting on March 20th or at a subsequent meeting." We received no reply to this letter and no invitation to appear before the task force.

SURVEY CONDUCTED BY THE CHAIRMAN OF THE AD HOC TASK FORCE ON PUBLICATIONS AND COMMUNICATIONS

In March 1992, the chairman of the Ad Hoc Task Force designed, implemented, and analyzed his own personal survey of what he characterized as key Society members. We, of course, raised the obvious questions about this survey:

- Why a new survey if the Member Needs Survey was supposedly valid?
- Can a survey designed, implemented, and analyzed by someone with strong personal opinions be statistically valid and reliable?

In addition, this survey population included the non-physician executive directors of county medical societies who are not able to evaluate a clinical and scientific journal, a fact which some of them candidly confirmed.

We were extremely disturbed by the fact that the chairman of a task force charged with an objective evaluation of society publications should have designed, implemented, and analyzed his own survey. Given his strong bias against the *Journal*, there was a high risk that the results of this second survey would be both biased and invalid. The survey, as constructed, was expected to produce negative results with regard to the *Journal*, and it did.

THE 1992 HOUSE OF DELEGATES MEETING

Many Society members in addition to the members of your Publications Committee were deeply concerned by the actions of the chairman of the Task Force on Publications and Communications. **In refusing to accept input from either the *Journal's* editorial staff or from the Publications Committee, he narrowed the information base available to the members of the task force. In addition, some members of the task force itself were concerned with the speed with which the group was being moved forward in the direction of recommending the transformation of the *Journal* into a tabloid.**

These broad and collective concerns led to the introduction into the House of Delegates of two resolutions recommending the continuation of the *Journal* as a quality, peer-reviewed scientific journal. These resolutions, 92-59 and 92-85, were respectively introduced by the Nassau County Medical Society and the Seventh District Branch. Shortly after their submission to the Speaker of the House and well before the actual annual meeting, the chairman of the task force contacted the proposer of the Seventh District Branch resolution and attempted to get him to withdraw the resolution. The Seventh District Branch did not withdraw the resolution but went ahead to present their case before the house.

At the reference committee meeting, many strongly spoke for the *Journal*. The chairman of the task force tried to convince listeners that the adoption of the two resolutions would impede the work of the task force. He also reassured listeners that the purpose of the task force was not to abolish the *Journal*. However, he did not bother to tell them that his intent was the transformation of the *Journal* into a socio-economic tabloid. Many spoke in favor of the resolutions supporting the *Journal* at the reference committee, which recommended adoption by the House of Delegates.

During the House session where the two resolutions were considered, it was clear that there was very strong support for the *Journal* as a peer-reviewed clinical and scientific publication. The concern of many who support the *Journal* was that referral of the two resolutions by the House to the Council would remove the decision concerning the *Journal* from the House of Delegates, the Society's supreme governing body. The Publications Committee and many members believe that so important an issue as the *Journal* must be decided by the House of Delegates, with all due respect to the Council.

An amendment was introduced to resolution 92-85, stating: "That any recommendation to discontinue or alter the peer-reviewed status of the *New York State Journal of Medicine* by the Task Force on Communications and Publications be submitted to the 1993 MSSNY

House of Delegates meeting for deliberation before any final decision is made." This amendment was introduced in order to guarantee that final decisions concerning the future of the *Journal* would rest with the next House of Delegates. Thus, when the House referred the resolutions to the Council, it explicitly stated that it would be involved in any final decision concerning the *Journal*.

ATTEMPTS TO CIRCUMVENT THE WILL OF THE HOUSE OF DELEGATES

In August 1992, the chairman of the task force and others attempted to interpret the Society By-Laws as giving the Council absolute authority over the *Journal*, in spite of the amendment to resolution 92-85. Aware of this, some members contacted the Speaker of the House of Delegates to emphasize that on this matter, the will of the House was explicit and final. The House had, in effect, instructed the Council to refrain from any actions concerning the *Journal* and to report back at the 1993 meeting. Consequently, this attempt by the task force chairman to bypass the will of the House was unsuccessful.

RECOMMENDATIONS OF THE AD HOC TASK FORCE

The chairman of the task force then went before the Council of the Society on September 10, 1992, with a resolution that as written would have immediately transformed the *Journal* into a tabloid to be published under the supervision of his task force. The Council wisely declined to approve this resolution. Rather, it authorized the publication of a prototype tabloid under the supervision of the task force beginning in December and concurrently with the *Journal*. The Council postponed consideration of the two 1992 House of Delegates resolutions concerning the *Journal*.

THE UNIQUENESS OF A PEER-REVIEWED CLINICAL AND SCIENTIFIC JOURNAL AND THE PLETHORA OF MEDICAL TABLOIDS

As was raised at a recent meeting of the Society's medical student section, the *Journal* is unique. It is the only peer-reviewed clinical and scientific journal published in New York State primarily for New York State physicians.

There are many socio-economic medical tabloids already in circulation in New York State. Those published in the state primarily for New York State physicians include the following:

<i>New York Doctor</i>	(circulation 15,000)
<i>New York State Medical News</i>	(circulation 42,000)
<i>The Medical Herald</i>	(circulation 50,000)

In addition to these, there are national tabloids such as *Physician's Weekly*, *American Medical News*, and the *Physician Observer*. The latter, put out by the American College of Physicians, has a circulation of 14,000 in New York State. Thus, physicians in New York State are already inundated with many socio-economic medical tabloids. Three of these already focus on local New York State socio-economic medical issues. A tabloid published by the Society will be competing in a very crowded arena.

SUPPORT FOR THE JOURNAL

During the past year, many have written to various Society officers in support of the *Journal* as a peer-reviewed clinical and scientific publication. In May 1992, all of the deans of New York State's medical schools collectively wrote to the Society's president expressing their strong support for the *Journal*, indicating to him its great value to faculty and students.

Many readers know of the two important resolutions of support introduced into the 1992 House of Delegates by Nassau County and the Seventh District Branch, and of the three resolutions of support by the First District Branch. Readers regularly write in supporting the *Journal*, and this, coupled with our 1987 readership survey, leave no doubt that members want a peer-reviewed clinical and scientific journal and want it to be continued as such.

A COST-EFFECTIVE PROPOSAL FOR COVERING SOCIETY BUSINESS AND SOCIO-ECONOMIC ISSUES IN THE JOURNAL

The Committee on Publications, Library, and Archives understands the importance of society news and socio-economic issues for members. *News of New York*, the Society's newsletter, provides succinct coverage of important topics. Its attractive layout and brevity ensure high levels of readership.

We would like to suggest that at various intervals an insert of several pages be prepared by the Division of Communications, covering in-depth important society news and activities, as well as socio-economic issues. These inserts, which could complement *News of New York*, could be printed on a distinctive paper, and placed in the *Journal* at either the beginning, the end, or in the centerfold. Their inclusion in the *Journal* would ensure high readership levels. The cost of printing a 16-page insert would be on the order of \$8,000, far less than that of printing a tabloid. Even if such inserts were placed in each of the *Journal's* annual 12 numbers, the cost would still be covered by present levels of *Journal* profit.

This option of placing inserts covering socio-economic issues and society activities in the *Journal* would enable the Society to retain its premiere peer-reviewed clinical and scientific journal, while expanding communication with members on socio-economic issues. These inserts would benefit from their association with a peer-reviewed scientific and clinical journal in terms of readership levels and from the *Journal's* advertising income.

CONCLUSIONS

The Society should periodically evaluate its publications and how it communicates with its members. To be valid, such evaluations must be based on comprehensive information, open and due process that provides for the expression of a range of informed views and valid readership surveys free of bias and statistical flaws. The 1987 readership survey of the *Journal* resulted in a statistically valid response rate and assessments of the *Journal* indicating that members want and value a peer-reviewed clinical and scientific journal. The recent Member Needs Survey, with its unreliable 28.24% response rate, produced different results. We and many

other members of the Society are greatly troubled that the inquiry of the Task Force on Publications and Communications was narrowly framed within the context of this latter survey. It would be a serious error for the House of Delegates and the Society to make a decision about the *Journal* on the basis of such a survey.

The *New York State Journal of Medicine* is a highly respected and widely quoted journal that produces an annual profit. It was recently honored by the Library of Congress as a medical journal of excellence and is ranked among the top 5% of peer-reviewed medical journals. It brings great respect and credibility to the Society, serves as an important link to young physicians and medical students, and is unique as the only peer-reviewed clinical and scientific journal published in New York State primarily for the state's physicians.

Expressions of support for the *Journal* have come over the past several months from all the deans of New York State's thirteen medical schools, from medical students, young physicians, busy practitioners, and from retired members.

Three medical tabloids are already published in New York State for the state's physicians. Most of us receive several medical tabloids that are national in circulation. As a tabloid, the *New York State Journal of Medicine* would lose much advertising income, find little original extra-society material to publish not already covered by other tabloids, and be a poor benefit of membership not

likely to retain some current members nor attract new ones.

A reasonable and cost-effective approach for increasing communication about society activities and socioeconomic issues is to develop inserts for the *Journal*. These inserts could cover specific topics in depth, be prepared by the Division of Communications, complement *News of New York*, and be printed on distinctive paper and placed in the *Journal*.

The *New York State Journal of Medicine* is entering its 93rd year and is not far from celebrating its centennial as a clinical and scientific publication. Medical tabloids are numerous and often have short life spans. Peer-reviewed clinical and scientific medical journals rated in the top 5% of such publications that are approaching their centennials are precious and rare. We hope that the Council and the House of Delegates will reflect on these facts as they decide the future of this valuable, respected, and venerable publication.

MILTON GORDON, MD

Chairman,

and the Members of the Committee on Publications,

Library, and Archives

Medical Society of the State of New York

420 Lakeville Road

Lake Success, NY 11042

Trends in AIDS mortality among residents of Puerto Rico and among Puerto Rican immigrants and other Hispanic residents of New York City, 1981–1989

BARBARA S. MENENDEZ, PhD; STEVE BLUM, PhD; TEJINDER P. SINGH, PhD;
ERNEST DRUCKER, PhD

ABSTRACT. This study contrasts the acquired immunodeficiency syndrome mortality experience of residents of Puerto Rico with that of New York City residents identified as either Puerto Rico-born and non-Puerto Rico-born Hispanics. Portions of the mortality data examined in this investigation update and extend the data previously published describing selected groups in New York City through the end of 1987 but which did not consider residents of Puerto Rico. The nine-year cumulative, age-adjusted acquired immunodeficiency syndrome mortality rate for males was found to be 5× higher among Puerto Rico-born New York City residents compared with residents of Puerto Rico (702/100,000 v 141/100,000) and 1½× greater than that of other male Hispanic New York City residents (447/100,000). In New York City, Puerto Rico-born females had higher age-adjusted mortality rates (121/100,000) than female residents of Puerto Rico (25/100,000) and other female Hispanic residents of New York City (70/100,000). Within five of the six age categories considered, acquired immunodeficiency syndrome mortality rates for adult males and females are higher for Puerto-Rico-born, New York City residents. Limitations of acquired immunodeficiency syndrome incidence data, as they pertain to persons of Puerto Rican ancestry, are discussed.

(NY State J Med 1993; 93:12–15)

Although it has been demonstrated that the acquired immunodeficiency syndrome (AIDS) epidemic disproportionately affects Hispanic populations relative to whites,¹ only since 1989 has the differential impact of AIDS among subgroups of the Hispanic population been addressed. In calling attention to differences in AIDS incidence rates and modes of transmission according to country of birth, a study comparing foreign-born Hispanic groups in the United States (US) demonstrated that Puerto Ricans who immigrated to the mainland were experiencing higher AIDS rates in relation to all other foreign-born Hispanic groups.² In addition, the high incidence of AIDS among Puerto Ricans was not limited to island-born immigrants; it also became manifest among Puerto Rico's (PR) resident population.

In 1990, PR had a higher incidence rate of AIDS among adult and adolescent males (131.5/100,000 population) and

among women (27.6/100,000) than of any of the 50 states of the US.³ Puerto Rican women have also had a higher proportion of AIDS cases caused by heterosexual transmission than any other race/ethnic female group in the US.⁴ Moreover, the San Juan PR metropolitan area had one of the highest AIDS incidence rates per 100,000 population compared to all US metropolitan areas with 500,000 or more inhabitants.⁵ This study updates and extends a previous AIDS mortality study,⁶ limited to the New York experience through 1987 and which did not include PR.

METHODS

The mortality data examined in this study are based on death certificate information for the years 1981–1989 and were provided by the PR Department of Health and the New York City (NYC) Department of Health. AIDS deaths were identified by International Classification of Diseases (ICD) codes 279.1 (deficiency of cell-mediated immunity), 136.3 (*Pneumocystis carinii*), and 173.9 (Kaposi's sarcoma); also included were deaths due to infections and cancers attributed to human immunodeficiency virus (HIV) infection (code 042) occurring after December 31, 1986.⁷ To conform with methods used by the NYC Department of Health to generate mortality summaries, deaths assigned ICD codes 043 and 044 (other HIV-related conditions) were excluded.

AIDS deaths among two NYC Hispanic groups were analyzed: among residents of NYC born in PR (NYC/PR-born) and other Hispanic residents of NYC (NYC/Hispanic). The NYC/Hispanic group comprised all Hispanics born anywhere except PR; those of Puerto Rican ancestry who were not born on the island would necessarily be included in the NYC/Hispanic group. Since 48% of NYC's Hispanic population between the ages of 25 and 44 is of such ancestry,⁸ it is conceivable that a large proportion of AIDS deaths in this group actually occurred among those of Puerto Rican descent. It is worth noting that death certificates do not routinely identify the ancestral national origin of US-born Hispanics.

Nine year (1981–1989) cumulative, age-specific, and age-adjusted AIDS mortality rates per 100,000 population were calculated for males and females in each of the three groups defined above. The 1980 US census served as the population base, whereas the 1970 US standard million population provided the set of weights for direct age-adjustment. Short-term trends in AIDS proportional mortality occurring among the three groups, by age and gender, were reviewed to characterize the epidemic's behavior between 1988 and 1989.

From Lehman College, Bronx, NY (Dr Menendez), the Office of Epidemiologic Research, New York City Department of Health (Dr Blum and Dr Singh), and the Department of Epidemiology and Social Medicine, Montefiore Medical Center, Bronx, NY (Dr Drucker).

Address correspondence to Dr Menendez, Department of Health Services, Lehman College, Bedford Park Boulevard West, Bronx, NY 10468.

RESULTS

Presented in Table I are the age-specific and age-adjusted, nine-year, cumulative AIDS mortality rates for residents of PR, PR-born residents of NYC, and all other Hispanic residents of NYC by gender. Rates were higher among PR-born male and female residents of NYC. These groups had higher age-specific mortality rates with the exception of the under-15 age group for males and the 25–34 age group for females. In both these cases, Hispanic residents of NYC had the higher rates. The highest age-specific mortality rates among males occurred in the aged 35–44-years category in each of the three ethnic groups, and the single highest rate occurred among PR-born male residents of NYC (2,453/100,000 population). Notably, while the rate for PR-born female residents of NYC was also highest in this age category, rates among females from the two remaining groups peaked at an earlier age. The age-adjusted rate per 100,000 population for PR-born male residents of NYC (702) was 5× higher than that of Puerto Rican male residents (141), and 1½× higher than that of Hispanic male residents of NYC (447).

Similar excesses were observed for PR-born female residents of NYC, whose age-adjusted rate per 100,000 population (121) was nearly 5× higher than that of Puerto Rican female residents (25) and approximately 1.7× greater than that of Hispanic female residents of NYC (70).

Table I further shows that among PR-born male and female residents of NYC, the number of AIDS deaths peaked in the aged 35–44-years category: 888 deaths (48% of all AIDS deaths) occurred among males, whereas 168 deaths (45% of all AIDS deaths) occurred among females. For the remaining groups, the largest number and proportion of deaths occurred

TABLE I. Age-specific and Age-adjusted* AIDS Mortality Rates per 100,000 Population† Among Puerto Rico Residents, and Puerto Rico-born and All Other Hispanic‡ Residents of New York City by Gender, 1981–1989

Age Group (yr)	Puerto Rico Residents		Puerto Rico-born NYC Residents		All Other Hispanic NYC Residents	
	Deaths	Rate	Deaths	Rate	Deaths	Rate
Males						
<15	29	5.6	2	15.5	56	28.3
15–24	102	34.3	40	204.8	78	69.3
25–34	846	387.7	531	1,523.5	841	1,090.8
35–44	773	455.9	888	2,453.5	619	1,363.6
45–54	234	180.7	316	1,163.3	245	778.5
55+	259	69.8	92	329.7	84	256.2
Total age adjusted rate (Standard error)	2,143 (3.08)	141.1 (3.08)	1,869 (17.01)	702.4 (17.01)	1,923 (11.09)	447.2 (11.09)
Females						
<15	21	4.2	5	38.4	43	22.5
15–24	32	10.3	17	71.9	29	23.4
25–34	199	80.4	124	265.8	256	284.7
35–44	105	55.1	168	369.7	86	163.1
45–54	25	17.2	50	145.1	12	29.9
55+	65	21.4	13	34.0	7	13.7
Total age adjusted rate (Standard error)	447 (1.20)	25.2 (1.20)	377 (7.80)	121.3 (7.80)	433 (3.49)	70.1 (3.49)

Data sources: NYC Dept. of Health and Puerto Rico Dept. of Health.

*Based on 1970 US standard million population yielding weights of .28492, .17441, .12257, .11361, .11427 and .19022 for age categories <15 through 55+.

†1980 US census data used for subgroup denominators.

‡Includes persons of Puerto Rican ancestry and persons of Hispanic origin (born inside or outside the United States).

among those in the aged 25–34-years category. Notice that the largest number of deaths among children under age 15 occurred among Hispanic residents of NYC (56 males and 43 females).

Table II presents the results of a Poisson regression analysis in which the relevant χ^2 test variate for the second-order joint effects of Gender $\times$ Origin $\times$ Age supports the finding that age-specific rates differ markedly across levels of one factor, say origin, with respect to age category and gender.

Table III displays AIDS mortality as a percentage of all deaths that occurred among residents of PR and the two other ethnic groups. Although the percentage of AIDS deaths among males in all three groups grew steadily over time, this trend was somewhat less uniform among females. The highest single percentages occurred in NYC residents, among both PR-born males and all other Hispanic males, with 18% in 1989.

Presented in Table IV by age, ethnic category, and gender for each of the three groups are the numbers of AIDS deaths that occurred between 1988 and 1989 as a percentage of all deaths during this period. Regarding PR-born male residents of NYC, nearly 44% of all decedents between the ages of 25 and 34 died of AIDS. Conversely, AIDS accounted for approximately 30% of all deaths in residents of PR and other Hispanic residents of NYC in this same age group. Perhaps most striking is that the percentage of deaths caused by AIDS among PR-born male residents of NYC between ages 15 and 24 years was 6× larger than for males of similar age in the other two groups. Furthermore, as a percentage of all deaths among females, AIDS was highest for those between ages 25 and 34 years.

DISCUSSION

This investigation compared the AIDS mortality rates in PR, a rather diverse territory, including both urban and rural areas, with rates among inner city groups in NYC, a highly urban setting. The lower age-specific and age-adjusted AIDS mortality rates among residents of PR may be explained by the fact that AIDS rates are generally higher in large cities than in small cities or rural areas.⁹ Rates for AIDS in states or territories would be lower than the rates in large cities within those states or territories because the rates of the former are diluted by inclusion of smaller cities and rural areas. This could explain why the rate in PR (a territory) is lower than the rate in NYC (a large city).

That AIDS mortality rates in PR were lower than those in NYC may be due to the possibility that certification of an AIDS death on the island remains somewhat less comprehensive than in NYC. During the period examined, PR

TABLE II. Results of Poisson Regression Analysis of Age-specific Rate Data* Presented in Table I†

Factor	Degrees of Freedom	Partial Wald χ^2
Gender	1	527.6
Origin	2	471.8
Age	5	1,853.8
Gender $\times$ origin	2	11.1
Gender $\times$ age	5	144.5
Origin $\times$ age	10	106.5
Gender $\times$ origin $\times$ age	10	54.6
Omnibus statistic: ($H_0: \beta = 0$)	35	11,972.5

*The "response" variable is $\log(\text{Rate}_{\text{age-specific}}/10^5)$.

†"Full" model — 2 $\times$ 3 $\times$ 6 design.

TABLE III. Trends in AIDS Deaths as a Percentage of All Deaths Among PR Residents, and PR-born and All Other Hispanic* Residents of New York City by Gender, 1984–1989

Year	PR Residents			PR-born NYC Residents			All Other Hispanic NYC Residents		
	Total Deaths	AIDS Deaths	AIDS as %	Total Deaths	AIDS Deaths	AIDS as %	Total Deaths	AIDS Deaths	AIDS as %
Males									
1984	12,461	50	0.4	2,069	107	5.2	1,704	95	5.6
1985	13,466	82	0.6	2,182	164	7.5	1,651	172	10.4
1986	13,734	140	1.0	2,433	297	12.2	1,872	267	14.3
1987	14,047	390	2.8	2,608	357	13.7	2,070	346	16.7
1988	14,648	632	4.3	2,680	413	15.4	2,691	456	17.0
1989	15,243	819	5.4	2,760	490	17.8	2,956	534	18.1
Approximate annual % increase ($\Delta\%$) [†]		65%			23%			17%	
Females									
1984	9,284	12	0.1	1,503	23	1.5	1,052	23	2.2
1985	9,748	17	0.2	1,546	33	2.1	1,045	21	2.0
1986	9,690	27	0.3	1,639	45	2.8	1,131	58	5.1
1987	9,917	64	0.7	1,682	78	4.6	1,145	53	4.6
1988	10,374	160	1.5	1,902	96	5.1	1,485	127	8.6
1989	10,744	148	1.4	1,823	89	4.9	1,570	147	9.4
Approximate annual % increase ($\Delta\%$) [†]		66%			25%			35%	

Data Sources: NYC Department of Health and Puerto Rico Department of Health.

*Includes persons of Puerto Rican ancestry and persons of Hispanic origin (born inside or outside the United States).

[†]Estimated by weighted least-squares exponential regression of $\log_e$ (%-of-deaths) on year where, based on a McLaurin's series expansion, descriptive beta coefficient β is translated: $\Delta\%_{\text{annual}} = 100(\exp[\beta] - 1)$. Not intended for projection.

reported 2,590 AIDS deaths and 3,233 AIDS incident cases. In contrast, NYC reported 2,245 AIDS deaths but only 695 AIDS incident cases among its PR-born residents. PR's AIDS incidence-to-mortality ratio (1.25) therefore suggests that the island's reporting of AIDS incidence may be more reliable than its reporting of AIDS deaths. Conversely, NYC's AIDS incidence-to-mortality ratio (0.31) suggests that cases of AIDS among city residents born in PR may well have been misclassified geographically (ie, PR-born NYC residents were misclassified as US-born).

These inverse ratios suggest that certain individuals diagnosed with AIDS in PR will eventually move to NYC to obtain better medical treatment, thereby resulting in a smaller number of AIDS deaths occurring on the island. Puerto Ricans have been the Hispanic group most affected by the "air" propagation of AIDS. This is clearly the result of strong social and cultural ties that bind "mainland" with "island" Puerto Ricans, as well as the availability and convenience of unrestricted low-cost air travel between NYC and PR.

TABLE IV. AIDS Deaths as a Percentage of All Deaths Among PR Residents, PR-born and All Other Hispanic* Residents of New York City, by Age and Gender, 1988–1989

Age Group (yr)	PR Residents			PR-born NYC Residents			All Other Hispanic NYC Residents		
	Total Deaths	AIDS Deaths	AIDS as %	Total Deaths	AIDS Deaths	AIDS as %	Total Deaths	AIDS Deaths	AIDS as %
Males									
<15	1,770	15	0.8	14	2	14.3	515	29	5.6
15–24	937	67	7.2	110	48	43.6	612	35	5.7
25–34	1,934	570	29.5	557	248	44.5	1,365	428	31.4
35–44	2,332	547	23.5	1,146	421	36.7	985	339	34.4
45–54	2,471	156	6.3	981	176	17.9	564	114	20.2
55+	21,447	96	0.4	2,632	41	1.6	1,606	45	2.8
Subgroup total	30,891	1,451	4.7	5,440	936	17.2	5,647	990	17.5
Females									
<15	581	18	3.1	21	3	14.3	439	21	4.8
15–24	306	24	7.8	46	4	8.7	136	26	19.1
25–34	548	134	24.5	158	53	33.5	453	168	37.1
35–44	774	83	10.7	338	82	24.3	289	55	19.0
45–54	1,160	18	1.6	400	29	7.3	223	9	4.0
55+	17,749	33	0.2	2,762	7	0.3	1,515	5	0.3
Subgroup total	21,118	310	1.5	3,725	178	4.8	3,055	284	9.3

Data Sources: NYC Department of Health and PR Department of Health.

*Includes persons of Puerto Rican ancestry and persons of Hispanic origin (born inside or outside the US).

If the data on AIDS incident cases among NYC's PR-born are incorrect, they may also be incorrect for other PR-born persons living elsewhere in the US. In this regard, it is important to remember that the AIDS data collection protocol used by the Centers for Disease Control (CDC) requires place-of-birth information for all reported incident cases. Until the spring of 1992, the CDC data collection form provided an explicit country-of-birth check-off for persons born in the US, Canada, the Dominican Republic, Haiti, and Mexico. For persons born in any other country, the name of their country had to be specified in a blank space next to the check-off box labeled Other. Because persons born in PR are US citizens and because PR was not an explicit check-off option for this item, confusion may have arisen as to whether those born in PR were to be classified in categories Other or US. The CDC introduced a new form in early 1992, in which the place of birth in "US dependencies and possessions (including PR)" is listed as a check-off box. This should prevent PR-born persons from being misclassified as born in the US. The AIDS data collection form used in PR has now also listed PR as an option under the place-of-birth item.

It is likely that additional AIDS deaths occurred among inner city intravenous drug users (IVDUs), many of whom are of Puerto Rican ancestry, but were not classified as HIV-related deaths.¹³ Indeed, when the CDC definition was expanded in August 1987, the largest increase in incidence was observed among IVDUs.¹⁴ Presumptive diagnoses, now admissible under this expanded definition, are used more frequently in PR than in NYC. PR is thus more likely to classify IVU-related deaths as AIDS deaths when certain symptomatology is present before death. This may account for the 172% increase in the number of AIDS deaths occurring in PR between 1986 and 1987 (from 167 to 454 deaths), compared with increases of 27% and 23% that occurred among PR-born and other Hispanic residents of NYC, respectively, during that period. The difference in the rates of increase that occurred in PR and NYC suggests that AIDS underreporting among IVDUs was greater in PR than in NYC before the expanded definition. Intravenous drug use accounts for a larger proportion of AIDS incident cases among residents of PR (60%) than among Hispanic residents of NYC (53%) and NYC blacks (48%) or, for that matter, all US Hispanics (39%) and all US blacks (35%).

The number of AIDS deaths among Puerto Ricans in NYC was actually greater than the number presented here because AIDS deaths among persons of non-island born Puerto Rican ancestry were grouped with NYC/Hispanics. This is primarily because the death certificate did not require information on national ancestry until the latter part of the period under study. However, because 62% of NYC's Hispanic population was of Puerto Rican origin (ie, born in PR or of Puerto Rican ancestry) according to 1980 census figures, it is reasonable to assume that a considerable number of AIDS deaths reported for NYC/Hispanics

actually occurred to persons of Puerto Rican ancestry.⁸ An examination of 1989 AIDS deaths among the foreign-born in PR revealed that 76% ($n = 84$) occurred to persons born in the US. It is thus possible that an unknown number of second generation Puerto Ricans resided on the mainland, where they were diagnosed with AIDS, and later returned to PR where they died.

It should be recognized in any proportional mortality study that because the percentages of deaths in any group of interest must sum to 100, when other competing causes of death are low, the cause of interest (here, AIDS) will be high. It follows that a high proportion of deaths may not necessarily be associated with a high population rate. Among all PR-born males residents of NYC, for instance, the highest age-specific rate of AIDS occurred among those between ages 35 and 44 years. As a proportion of all deaths, however, the largest proportion attributed to AIDS occurred among those between ages 25 and 34 years. It is nevertheless striking that among residents of PR, about a third of all male deaths and a quarter of all female deaths that occurred in the aged 25–34-years group were attributed to AIDS.

Acknowledgments. This research was supported in part by a grant from the City University of New York, PSC/CUNY Research Award Program #661257. The authors thank Ms Susan Vogue, Social Sciences Librarian at Lehman College, and Dr Ruth Reyes Castillo and Ms Carmen Ayoroa from the Puerto Rico Department of Health.

REFERENCES

1. Selik R, Castro K, Pappaioanou M: Racial/ethnic differences in the risk of AIDS in the United States. *Am J Public Health* 1988; 78:1539–1545.
2. Selik R, Castro K, Pappaioanou M, et al: Birthplace and the risk of AIDS among Hispanics in the United States. *Am J Public Health* 1989; 79:836–839.
3. Centers for Disease Control: Update: Acquired immunodeficiency syndrome—United States, 1981–1990. *MMWR* 1991; 40:358,363,369.
4. Statistical Report. HIV/AIDS Surveillance Report. Oficinas de Centro de Asuntos de SIDA. Puerto Rico, June 1990.
5. HIV/AIDS Surveillance: US Department of Health and Human Services, Public Health Service, CDC, National Center for Infectious Diseases, Division of HIV/AIDS, July 1991.
6. Menendez BS, Drucker E, Vermund SH, et al: AIDS mortality among Puerto Ricans and other Hispanics in New York City, 1981–1987. *J Acquir Immune Defic Syndr* 1990; 3:644–648.
7. World Health Organization Collaborating Center for Classification of Diseases for North America: HTLV-III/LAV Infection Codes: Official Authorized Addendum, Effective 1 October 1986. International Classification of Diseases, 9th Rev Clinical Modification, vol 1&2, Update. Rockville, MD: National Center for Health Statistics, 1986.
8. Census of population: General population characteristics—New York. US Department of Commerce. Washington, DC: US Bureau of the Census, 1983: PC80-1-B34.9.
9. Centers for Disease Control: HIV/AIDS Surveillance Report, April 1992:7.
10. Personal communication: Division of HIV/AIDS Surveillance, New York City Department of Health, September 1991.
11. Stoneburner RL, Des Jarlais DC, Benezra D, et al: A larger spectrum of severe HIV-1-related disease in intravenous drug users in New York City. *Science* 1988; 212:916–919.
12. Selik MR, Buehler JW, Karon JM, et al: Impact of the 1987 revision of the case definition of acquired immunodeficiency syndrome in the United States. *J Acquir Immune Defic Syndr* 1990; 3:73–82.
13. Census of Populations: General Population Characteristics—New York. US Department of Commerce. Washington, DC: US Bureau of the Census, 1983: PC80-1-B34.

Anti-convulsant drugs, smoking, and body weights in psychiatric in-patients

BHARAT S. SHAH, MD, HAROLD RATNER, MD

ABSTRACT. Some anti-convulsant drugs have a calming effect that may potentially be used to reduce cigarette smoking. A cross-sectional study, including all 100 psychiatric in-service patients receiving various anti-convulsant drugs and their age- and sex-matched controls, was done. The intensity of their daily cigarette smoking and their body weights were recorded. Of the patients, 25% were non-smokers. Of the 22 patients on phenytoin, eight were non-smokers as opposed to three in the control group. Two thirds of the phenytoin group patients were either non-smokers, or were nominal smokers. As opposed to this, of the control patients and those on other anti-convulsants, two thirds were either moderate or heavy smokers. The phenytoin group of patients weighed less than the controls (149 v 163 lbs). Valproic acid therapy was associated with a significantly higher body weight and with more smoking. Clonazepam's effect was similar to valproic acid, but carbamazepine did not show any relationship either with smoking or with body weights. Therapy with phenytoin is associated with a lower prevalence and a lower intensity of cigarette smoking, together with lower body weights in psychiatric in-patient population.

(NY State J Med 1993; 93:16-17)

High prevalence of cigarette (cgs) smoking in psychiatric in-patients is well recognized, but not well explained. Among other things, it may be related to anxiety and restlessness. To control agitation in these patients, relatively non-sedating anti-convulsant drugs (carbamazepine, valproic acid, clonazepam, and in the past, phenytoin) have been used. A calming or "normalizing" effect of phenytoin has been noted¹ for a few decades now. Can this supposedly calming effect of phenytoin and possibly other anti-convulsant drugs be exploited to control smoking? In addition, will it help prevent the weight gain that follows smoking cessation in some people?

To explore this hypothesis, that is, to determine whether treatment with these drugs is associated with any difference in smoking habit, in body weights, or in both, we did a cross-sectional observational study. Anxiety may lead one to resort to alcoholism, drug abuse, and excessive sex as well, but these aspects were not explored in this study.

METHODS

At the Manhattan Psychiatric Center, in June 1991, there were 100 patients who, in addition to several medical and psychiatric medications, were receiving phenytoin, carbamazepine, clonazepam, or valproic acid for seizures or aggres-

sive behavior or both. One hundred individually age- and sex-matched patients, who were also receiving other medications but none of the drugs listed above, were included in the study as controls. Those patients who were deemed to be physically unable to smoke because of severe medical conditions (eg, bed-ridden patients) were to be excluded from the study.

The body weights were the latest ones recorded within the past 30 days. Information about the smoking habits was obtained from the patients themselves and from the staff members from whom they get a "light" for their cigarettes. The intensity of smoking in each patient was broadly categorized as (A) non-smoker, (B) nominal smoker (1-5 cgs/day), (C) moderate smoker (6-20 cgs/day), and (D) heavy smoker (21 or more cgs/day). These categories are descriptive only, and they do not imply any value judgment as to the merit of smoking.

On a few hospital wards, according to the local policies, smoking was restricted to certain designated hours only, thereby effectively limiting it to a maximum of 9 cgs/day. This would expand the category (C) at the expense of (D) but would have no effect on the categories (A) and (B). Therefore, the latter two categories were grouped together, as were the former ones.

The smoking habit of each patient was compared with that of the matching patient, using McNemar's χ^2 test for presence or absence of the factor "smoking more than five cigarettes a day," that is, categories (C) and (D), for the reason mentioned above. Similarly, body weight of each patient was compared using McNemar's test for the factor "weighing more than 150 lbs." Odds ratios were computed for each of the two factors.

RESULTS

There were 100 patients, 63 men and 37 women, aged 36-78 years, in each group. No eligible patient had to be excluded on the basis of physical condition. Of the 200 patients, 75% were smokers. Their smoking intensities are shown in Table I. In contrast to the controls and other anti-convulsant drugs, the phenytoin group had two thirds of the patients in the non-smoker or nominal smoker category. The phenytoin data have been reported by us previously.² McNemar's test showed χ^2 value = 4, df: 1, $p < 0.05$.

The odds ratio for a patient (Table I) on phenytoin being a moderate or a heavy smoker was 0.125. The ratio for patients on clonazepam was 2.00, and for valproic acid group it was 2.75. For carbamazepine, it was slightly more than one.

As shown in the table, phenytoin group of patients, on an average, weighed less than the controls. On the other hand, the valproic acid group weighed significantly more than the controls (McNemar's $\chi^2 = 8.0$, $p < 0.01$). The Odds Ratios for one to weigh more than 150 lbs are also shown in the table, with phenytoin having the lowest, and valproic acid having the highest odds. The clonazepam group also had a high ratio. Carbamazepine group presented slightly higher odds for both factors.

From the Medical Services of the Manhattan Psychiatric Center Wards Island Complex, New York, NY 10035.

Address correspondence to Dr B. Shah, Attending Internist, Department of Medicine, Woodhull Medical and Mental Health Center, 760 Broadway, Brooklyn, NY 11206.

TABLE I. Body Weights and Smoking Habits While on Anticonvulsant Therapy

Group	No. Patients (Controls)			
	Phenytoin	Carbamazepine	Valproic Acid	Clonazepam
A	8 (3)	10 (8)	6 (10)	1 (2)
B	6 (4)	4 (6)	2 (4)	0 (0)
C	6 (8)	12 (16)	11 (10)	4 (2)
D	2 (7)	15 (11)	12 (7)	1 (2)
Total	22 (22)	41 (41)	31 (31)	6 (6)
Odds ratio for smoking > 5 cigarettes/day	.125*	1.22	2.75	2.00
Weight (lb)	149 (163)	163 (161)	169 (149)	170 (151)
Standard deviation	35 (43)	37 (44)	30 (31)	32 (37)
Odds ratio for weighing > 150 lb	0.43	1.37	13.0†	2.0

*Significant at $p < 0.05$.

†Significant at $p < 0.01$.

Four patients from the phenytoin group received one more anti-convulsant drug: phenobarbital (three patients) and primidone (one patient). One additional patient received all these three drugs. The data from phenobarbital and primidone are not presented here because of the very small number of patients and also because these patients were also getting phenytoin.

DISCUSSION

Cigarette smoking is public health enemy number one and is all pervasive in the psychiatric population. Of the patients studied, 75% were smokers, which is about three times the national average. In this patient population, the lower prevalence and the lower intensity of smoking observed in association with phenytoin therapy are striking and these cannot be ascribed to the chance alone. This study was not designed to look into the various other important factors affecting the smoking behavior: disease conditions, other drug addictions, drug therapies and their side effects, and so forth.

It is interesting that treatment with carbamazepine, valproic acid, and clonazepam (a benzodiazepine), commonly used to treat aggressive behavior, was associated with virtually no alleviating effect, whereas that with the less frequently used drug, phenytoin, was associated with significant alleviation of smoking behavior.

Phenytoin is structurally similar to the barbiturates, but unlike the latter, it is neither sedating nor habit forming. It does have some well-recognized side effects. Even though a few of the patients receiving phenytoin were also getting primidone and phenobarbital, the lesser amount of smoking observed is not attributable to the latter. They are actually known to increase smoking.³ Seizures by themselves are not an important factor, since other anti-convulsant agents did not show any alleviating effect.

The lower body weight (Table I) of the phenytoin group is also interesting. Weight gain is a major concern for the smokers, especially women, who are thinking about quit-

ting.⁴ If phenytoin can help achieve smoking cessation without subsequent or consequent weight gain, it may turn out to be exactly what we need. It is free from the drawbacks of nicotine delivery systems, as it does not contain nicotine. Low cost, a good safety record, and a lack of sedation or habituation may make it an ideal agent for smoking cessation. The higher body weight associated with valproic acid has been reported before.⁵

A word about how this study came about. One of us (BSS) is a pulmonary internist, and having been impressed by the amount of smoking in our psychiatric hospital, was planning to start a study of smoking. At that time, he had read Jack Dreyfus's¹ book describing a number of uses of phenytoin, almost all based on the membrane-stabilizing property of the drug. Mainly, the "calming" effect of phenytoin caught the reader's eye.

It is possible that the calming effect of phenytoin removes the craving for nicotine and suppresses the feeling of deprivation, thereby preventing the consequent overeating and the weight gain. This raises several interesting questions of basic science that only more data can answer. The possible role of phenytoin as a weight-reducing diet drug also needs to be explored.

The companion volume to Dreyfus's book, listing 3,100 references,⁶ did not contain any mention of nicotine or smoking. A further literature search revealed that although serum phenytoin level is not affected by smoking, nicotine metabolism is impaired by phenytoin.⁷ Future studies will have to sort out the relative contributions of this effect of phenytoin, vis-à-vis its calming or "normalizing" effect. In addition, association is not causation, and a cross-sectional study such as the present one cannot shed any light on changes in the smoking pattern of a given individual. Only a prospective, placebo-controlled, double-blind study can help.

In conclusion, we have presented data to show that in the psychiatric in-patient population studied, therapy with phenytoin is associated with a lower prevalence and a lower intensity of smoking, together with a lower body weight. Treatment with valproic acid is associated with a higher level of all these. Treatment with clonazepam showed associations similar to those shown by valproic acid, albeit to a lesser degree, whereas carbamazepine therapy showed no such apparent associations.

REFERENCES

1. Dreyfus J: *A Remarkable Medicine has been Overlooked*. New York, Dreyfus Medical Foundation, 1981.
2. Shah BS, Ratner H: Phenytoin and smoking. [letter] *N Y State J Med* 1992; 92:71-72.
3. Henningfield JE: Nicotine. An old fashioned addiction, in Cohen M (ed): *The Encyclopedia of Psychoactive Drugs*. New York, Chelsea House Publishing, 1985; p 71.
4. Williamson DF, Madans J, Anda RF, et al: Smoking cessation and severity of weight gain in a national cohort. *N Eng J Med* 1991; 324:739-745.
5. Strakowski SH, Hudson JI, Keck PE Jr, et al: Four cases of obstructive sleep apnea associated with treatment resistant mania. *J Clin Psychiatry* 1991; 52:156-158.
6. Smith BH, Bogoch S, Dreyfus J: *The Broad Range of Clinical Use of Phenytoin: Bioelectrical Modulator*. New York, Dreyfus Medical Foundation, 1981.
7. Lubawy WC, Kostenbawder HB, McGovern JP: In vivo and in vitro alteration of nicotine metabolism by the major metabolite of phenytoin. *Res Commun Chem Pathol Pharmacol* 1978; 19:257-269.

State experience with Medicare hospital mortality: How does New York State compare?

JOE FEINGLASS, PhD; LARRY MANHEIM, PhD; STEPHEN SHORTELL, PhD;
EDWARD F. X. HUGHES MD, MPH

ABSTRACT. 1987 Medicare hospital mortality statistics for 255 New York hospitals (including 57 hospitals in New York City) were compared with 4,617 hospitals located in other states. An analysis of covariance examined how overall Medicare hospital mortality rates differed across states; these rates were adjusted for expected mortality, hospital bed size, and major teaching status. This study tested for the hypothesis that New York State had an average 30-day post-admission Medicare mortality rate significantly different from the mean hospital mortality rate for all states. The results indicated that New York State was -0.43 percentage points below the average risk-adjusted mortality rate of the other states ($p < 0.0001$). Although it remains speculative to what extent differences in adjusted Medicare hospital mortality are a function of quality of care, these results indicate that New York's historically high level of hospital regulation has not resulted in inferior patient outcomes.

(NY State J Med 1993; 18-21)

Concern about the extent to which recent regulatory or competitive pressures on hospitals have affected patient outcomes has led to intensified scrutiny of hospital mortality rates. National interest in New York State Medicare hospital mortality rates arose, in part, from the negative publicity accompanying the 1986 public release of individual hospital Medicare mortality statistics by the Health Care Financing Administration (HCFA). The initial HCFA mortality data, based on inpatient death rates, were interpreted by some as suggesting that quality of care was inferior in hospital in highly regulated states like New York, which also had longer average lengths of stay.

Several factors contributed to the early belief that New York State mortality rates were worse overall than those of other states: for example, early HCFA rates showed New York State with very high Medicare mortality relative to other states.¹ However, early HCFA mortality data were based on a flawed model of expected mortality, which has subsequently been modified. In addition, the initial publicity on the mortality data release put too much emphasis on the fact that New York appeared to have a larger number of hospitals designated as high-mortality statistical "outliers" than other states. Studies by Gaumer et al² and Shortell and Hughes³ provided additional evidence that highly regulated states, like New York, may have had poorer hospital performance. These studies found that the stringency of state rate regulation and Certificate of Need

thresholds were associated with higher risk-adjusted hospital mortality rates in 1984.

Public concerns about deteriorating hospital quality are heightening, as New York hospitals experience increasingly severe financial pressures.^{4,5} During the 1980s, state rate regulation has been associated with significantly lower rates of hospital cost inflation in the all-payor Medicare waiver states, such as Maryland, New York, New Jersey, and Massachusetts.⁶⁻⁹ Critics of recent proposals for all-payor or Canadian-style health insurance often argue that such proposals will undermine quality by reducing the resources available to hospitals.

To determine what effects, if any, all-payor rate setting had on patient outcomes in New York, this study examines to what extent the 1987 Medicare hospital mortality rate in New York State differs from the rate in other states. Comparative patient outcome data from 1987 will reflect the long-term effects of New York's previous system of all-payor hospital rate regulation. Whereas HCFA mortality data for 1989 have just become available, the 1987 HCFA mortality data analyzed here represent the most relevant comparison of waiver state status. The risk-adjusted Medicare mortality experience in New York hospitals is compared with other states, controlling for hospital size and teaching status across states. This study is among the first efforts to use data derived from the more recent HCFA statistical model to document and examine the range of state-to-state differences in Medicare hospital mortality rates.

METHODS

Hospitals in Puerto Rico, the Virgin Islands, Alaska, and Hawaii were omitted from the sample. All hospitals in the remaining 48 states and the District of Columbia were then included in the analysis, if they had more than 100 Medicare patients discharges in 1987, and were categorized as being a general medical/surgical hospital with at least 25 beds and two physicians on the active staff, and if they had Medicare mortality rates of less than 25%. These conditions eliminate the smallest hospitals and hospitals with very high mortality rates caused by specialization into hospice-type programs.

Risk Adjustment of HCFA Mortality Data. The HCFA Hospital Mortality Tape, including both actual and expected mortality estimates, is used to examine how overall hospital mortality rates differ across states. The HCFA logistic regression model of expected mortality is based on the incidence of 30-day post-admission mortality divided by the number of each Medicare final admissions to that hospital within a calendar year. Death rates are computed separately for patients discharged in 17 diagnostic categories. The HCFA risk-adjust-

From the Center for Health Services and Policy Research, Northwestern University, Evanston, IL.

Address correspondence to Dr Feinglass, Center for Health Services and Policy Research, 629 Noyes St, Evanston, IL 60208.

ment model includes the presence of chronic disease comorbidities, the number of each patients' prior hospital admissions within six months (rated as high, low and undefined risk on the basis of principal diagnoses), patient age, sex, and whether the patient was transferred from another acute care hospital.¹⁰ In this study, estimates of each hospitals' expected mortality rate were computed from the HCFA confidence interval data.

Over the last four years, HCFA has refined its mortality release statistics, which are now based on a combination of Medicare claims and death certificate data from the Social Security Administration. HCFA computes expected death rates separately for patients discharged in 10 high-risk and 6 low-risk clinically homogeneous categories, which in 1988, included 65% of all patients and 72% of all 30-day post-admission deaths. Each hospital's overall expected mortality rate is computed on the basis of the volume of patients treated in each of the 16 diagnostic categories combined with the volume of patients with "undefined" diagnoses. More recently, HCFA has released three years of data on each hospital and published individual hospital characteristics and comments.

A number of studies, including several based on more detailed clinical data obtained from the New York Statewide Planning and Research Cooperative System database and manual chart reviews, have found that even the 30-day post-admission HCFA expected death model is biased, particularly in identifying hospitals designated as high-mortality statistical outliers.¹¹⁻¹⁴ A recent study found that models based on detailed clinical data and severity classifications were similar in terms of sensitivity and specificity for hospitals in the mid-range of mortality; however, the HCFA model tended to understate expected death for higher mortality hospitals.¹⁵ However, the 1988 HCFA case-severity measure, used for the 1987 Medicare mortality statistics analyzed here, is likely to be less biased in comparing overall state experience than in comparing individual hospital experience. This is because states are less likely to differ consistently on patient severity within diagnostic categories.

Comparing Other States to New York. Data on 1986 Medicare hospital mortality rates in the Northeast suggest that hospital volume, or the number of Medicare patients with a final calendar year discharge used to compute HCFA death rates, correlates with lower average mortality rates.¹⁶ Furthermore, hospitals treating higher volumes of the highest-risk HCFA diagnostic groupings also have significantly lower average death rates. The highest volume/lowest average mortality hospitals disproportionately tended to be large teaching hospitals, with higher concentrations of specialized, technology-intensive specialty services such as organ transplant, cardiac catheterization, specialized heart surgery, and magnetic resonance imaging facilities, as well as larger percentages of board-certified physician subspecialists and registered nurses. These have been found to be the most significant predictors of lower-adjusted Medicare mortality rates.¹⁷

To compare more fairly New York to other states or regions, hospital teaching status and bed size indicator variables are included as separate factors in an analysis of covariance. This is done to ensure that the comparison of state-level mortality rates accounts for the proportion of large teaching institutions in a given region. Data on statistical bed size and membership in the Council of Teaching Hospitals (a proxy for the existence of a significant postgraduate medical education program) were derived from the 1987 American Hospital Association Annual Survey of Hospitals.

Factors included in the analysis were hospital bed size (eight hospital bed size indicator variables), membership in the Council of Teaching Hospitals (COTH) (yes or no), and state (49 state variables). This model was estimated as a simple analysis of variance to measure state effects, controlling for the

HCFA measure of expected death rates based on case severity, hospital bed size, and teaching status. The hypothesis that hospital mortality rates in New York State, including or excluding New York City, were significantly different from the means of other states was tested. The analysis was weighted by the number of cases (last calendar year Medicare admissions) at each hospital divided by the sample hospital mean for all cases.

RESULTS

New York State had 255 hospitals the initial sample of 4,872 United States hospitals; 57 sample hospitals were located in New York City. Sample descriptive statistics for the variables used in the analysis are displayed in Table I.

Table II presents the number of hospitals in the sample for each state and the number and percentage of hospitals whose overall death rate exceeded the high and low outlier thresholds published by HCFA. Nine New York State hospitals (4.0%) were high death rate outliers, compared with the national average of 3.3%. New York also had 27 (12%) low outlier hospitals, compared with a national average of 4.9%. New York City had seven high (12.3%) and 12 low (21.1%) hospital mortality outliers. It should be noted that the number of HCFA-designated hospital outliers may to some extent simply reflect the size of a state's (or city's) hospitals, and thus, the statistical significance of differences. However, the fact that the percentage of low outlier hospitals greatly exceeds the percentage of high outlier hospitals suggests the overall hospital mortality experience of New York State is better than average.

Before entering the HCFA expected death rate variable, an initial model, including bed size, major teaching hospital status, and state location, was estimated to determine state rankings for raw, unadjusted Medicare death rates. This model explained only 14% of the variance in non-risk-adjusted hospital death rates. In this preliminary model of unadjusted death rates, the coefficient for New York State was 1.07 (ie, the model estimates that New York State hospital mortality was 1.07 percentage points above the simple average of state mortality rates ($p < 0.0001$)). The simple average of state mortality rates (the sum of the mortality rates for each state divided by 49) was 11.35%, so the predicted unadjusted New York State mortality rate was 12.42%.

When the HCFA expected death variable was entered into the same equation, the model explained 50% of the variance in overall death rates. In the case-severity-adjusted model, New York State was then -0.43 percentage points below the average of the other states, a statistically significant difference

TABLE I. Sample Frequencies and Descriptives

Total hospitals: 4872	
Mean number of final calendar year medicare discharges: 1199	
Mean death rate: 12.69%	
Mean HCFA expected death rate: 12.35%	
Mean HCFA 95% lower confidence interval, expected deaths: 9.47%	
Mean HCFA 95% upper confidence interval, expected deaths: 16.06%	
Hospitals affiliated with the council on teaching hospitals: 302 (6.2%)	
Bed size frequencies:	
6-24 beds	99 (2.0%)
25-49 beds	788 (16.2%)
50-99 beds	1,189 (24.4%)
100-199 beds	1,227 (25.2%)
200-299 beds	702 (14.4%)
300-399 beds	399 (8.2%)
400-499 beds	203 (4.2%)
500+ beds	265 (5.4%)

TABLE II. Number and Percent of High and Low Outlier Hospitals by State

State	Hospitals	High Outliers	Low Outliers
Alabama	118	2 (1.7)	3 (2.5)
Arizona	48	1 (2.1)	1 (2.1)
Arkansas	85	5 (5.9)	1 (1.2)
California	404	32 (7.9)	15 (3.7)
Colorado	48	1 (2.1)	4 (8.3)
Connecticut	35	0	4 (11.4)
Delaware	7	0	0
Wash., D.C.	10	1 (10.0)	2 (20.0)
Florida	211	7 (3.3)	8 (3.8)
Georgia	153	5 (3.3)	8 (5.2)
Idaho	31	1 (3.2)	0
Illinois	212	3 (1.4)	8 (3.8)
Indiana	112	3 (2.7)	0
Iowa	116	0	3 (2.6)
Kansas	115	2 (1.7)	6 (5.2)
Kentucky	100	1 (1.0)	8 (3.4)
Louisiana	127	2 (1.6)	7 (5.5)
Maine	40	1 (2.5)	3 (7.5)
Maryland	47	2 (4.3)	1 (2.1)
Massachusetts	97	1 (1.0)	15 (15.5)
Michigan	168	8 (4.8)	7 (4.2)
Minnesota	120	9 (7.5)	1 (0.8)
Mississippi	106	2 (1.9)	2 (1.9)
Missouri	131	7 (5.3)	7 (5.3)
Montana	32	0	9 (28.1)
Nebraska	71	1 (1.4)	0
Nevada	14	4 (28.6)	0
New Hampshire	27	0	2 (7.4)
New Jersey	85	4 (4.7)	2 (2.4)
New Mexico	31	1 (3.2)	1 (3.2)
New York	225	9 (4.0)	27 (12.0)
New York City	57	7 (8.1)	12 (21.0)
North Carolina	115	5 (4.3)	4 (3.5)
North Dakota	41	0	7 (17.1)
Ohio	178	1 (0.6)	6 (3.4)
Oklahoma	108	4 (3.7)	5 (4.6)
Oregon	65	2 (3.1)	1 (1.5)
Pennsylvania	210	2 (1.0)	14 (6.7)
Rhode Island	13	0	1 (7.7)
South Carolina	67	2 (3.0)	2 (3.0)
South Dakota	41	0	4 (9.8)
Tennessee	131	4 (3.1)	4 (3.1)
Texas	369	26 (7.0)	9 (2.4)
Utah	28	0	1 (3.6)
Vermont	15	0	0
Virginia	88	1 (1.1)	4 (4.5)
Washington	76	2 (2.6)	3 (3.9)
West Virginia	54	4 (7.4)	0
Wisconsin	52	0	10 (8.0)
Wyoming	53	0	0
Totals	4872	160 (3.3)	238 (4.9)

TABLE III. Rank Order of State Coefficients

State	Difference From Adjusted National Mean Death Rate*
North Dakota	-1.50 [†] (.38)
Montana	-1.42 [†] (.38)
South Dakota	-1.35 [†] (.38)
Massachusetts	-1.12 [†] (.15)
Maine	-1.10 [†] (.31)
Minnesota	-1.03 [†] (.21)
Connecticut	-0.72 [†] (.22)
Wyoming	-0.52 (.59)
Washington, D.C.	-0.52 (.40)
New York	-0.44 [†] (.10)
Rhode Island	-0.36 (.33)
Wisconsin	-0.35 [†] (.16)
New Hampshire	-0.29 (.36)
Vermont	-0.28 (.49)
Pennsylvania	-0.25 [†] (.10)
Kansas	-0.18 (.22)
Utah	-0.09 (.35)
Washington	-0.08 (.20)
Missouri	-0.07 (.15)
Ohio	-0.02 (.11)
Colorado	-0.01 (.25)
Mississippi	0.03 (.20)
New Mexico	0.05 (.35)
Louisiana	0.07 (.18)
Iowa	0.10 (.20)
Idaho	0.11 (.40)
Alabama	0.13 (.16)
Illinois	0.14 (.11)
Delaware	0.16 (.46)
Virginia	0.17 (.16)
Tennessee	0.19 (.15)
Florida	0.20 [†] (.10)
Kentucky	0.20 (.17)
Oregon	0.30 (.22)
Nebraska	0.32 (.28)
California	0.32 [†] (.09)
Oklahoma	0.40 [†] (.20)
Maryland	0.41 [†] (.19)
Michigan	0.42 [†] (.13)
Arizona	0.52 [†] (.21)
Georgia	0.54 [†] (.15)
New Jersey	0.56 [†] (.14)
North Carolina	0.56 [†] (.15)
Arkansas	0.58 [†] (.20)
Texas	0.69 [†] (.11)
South Carolina	0.86 [†] (.21)
West Virginia	0.89 [†] (.23)
Indiana	0.94 [†] (.15)
Nevada	1.76 [†] (.41)

*Standard errors are in parentheses.

[†]Significant at the 0.01 probability level, two-tail *t*-test.

[‡]Significant at the 0.05 probability level, two-tail *t*-test.

($p < 0.0001$). Hospital bed size and teaching status variables were significant ($p < 0.01$) and in the expected directions.

The coefficients and standard errors of each state in this model are given in Table III, which presents measures of each state's deviation from the overall state average, ranked from the state with the lowest to the state with the highest average adjusted Medicare mortality rate. Note the states at the extremes of the overall distribution are generally small states (eg, Nevada, South Dakota), whose experience may simply reflect random variation and peculiarities of their few and generally small hospitals. Two of the other three all-payor Medicare waiver states, New Jersey and Maryland, had higher than average adjusted mortality rates (0.56 and 0.41, respectively; $p < 0.05$). The final all-payor Medicare waiver state,

Massachusetts, had a significantly lower adjusted mortality rate (1.12, $p < 0.0001$). Thus, no clear pattern exists for these highly regulated states.

Separate variables for New York City and the rest of the New York State were then substituted for a single New York State variable. Before entering the HCFA expected death rate variable, the estimated mortality rate for New York City hospitals was 1.7 percentage points above the average for all states (with New York City considered as a separate state). The death rate for the rest of New York State was 0.65 percentage points above the all states' average. However, after controlling for expected death rate, New York City's risk-adjusted hospital mortality rate was -0.24 percentage points ($p = 0.11$) lower and the rest of New York State was 0.52 below

the all states average ($p < 0.0011$). The difference between the mortality rates for New York City and the rest of New York State hospitals was not statistically significant.

DISCUSSION

Serious methodological limitations have plagued the recent hospital mortality literature.¹⁷ In reference to evaluating hospital mortality in New York State, the most important of these limitations was the use of inpatient mortality, unadjusted for regional differences in average length of hospital stay, as an outcome measure. Jencks et al¹ found that New York had 99% higher average length of stay and 25% higher inpatient mortality than California in 1985. However, 30-days-from-admission mortality was 1.6% less in New York. Given changes in hospital case mix and medical records coding, the increased use of hospice care, do-not-resuscitate orders, and the earlier discharge of terminal patients to nursing homes, historical analyses based solely on hospital inpatient mortality trends complicate estimates of real changes in hospital quality of care.^{18,19}

The findings presented here demonstrate that in 1987, New York State hospitals' overall Medicare mortality was significantly better than average after controlling for HCFA's expected mortality measure. The difference between New York and the risk-adjusted Medicare mortality rates for other states persisted under alternative weighting (by the inverse of the variance of hospital expected death rates). The state level results reported here mirror the findings from an analysis of risk-adjusted, 30-day, post-admission mortality for Medicare patients discharged with new acute myocardial infarctions in 1987, which found that New York State had a 0.96 ratio of observed to expected deaths.²¹ The findings are also consistent with a regional analysis of more detailed area population and hospital structural characteristics.²²

It remains purely speculative as to whether the state differences in adjusted mortality rates reported here are in any way related to hospital reimbursement or regulatory policy. These data reveal that many relatively unregulated states had far worse risk-adjusted Medicare mortality rates than did highly regulated New York (or Massachusetts). However, it should be noted that widely differing population risk factors for disease have been well documented.²³ Some state-to-state differences are thus likely to be a function of still unmeasured differences in case severity. New York (and Massachusetts) hospitals' lower adjusted Medicare mortality experience may simply reflect unmeasured population and health status characteristics of the northeastern United States, as opposed to other regions, including the Mid-Atlantic region encompassing New Jersey and Maryland. Systematic differences in medical records coding (potentially related to New York's Medicare waiver status) may also have led to biased estimates of

Medicare expected mortality. Nevertheless, these results indicate that New York State's historically high level of hospital regulation has not resulted in inferior outcomes for patients.

Acknowledgments. This work was supported by a grant from the Hospital Association of New York State to the Center for Health Services and Policy Research, Northwestern University, and by grant no. HS06161a from the Agency for Health Care Policy and Research.

REFERENCES

1. Jencks SF, Williams DK, Kay TL: Assessing hospital-associated deaths from discharge data: the role of length of stay and comorbidities. *JAMA* 1988; 260:2240-2246.
2. Gaumer G, Poggio E, Coelen C, et al: Effects of state prospective reimbursement programs on hospital mortality. *Med Care* 1989; 27:724-736.
3. Shortell SM, Hughes EF: The effects of regulation, competition, and ownership on mortality rates among hospital inpatients. *New Eng J Med* 1988; 318:1100-1107.
4. Otten A: Intensive care units are rejecting patients because of crowding. *Wall Street Journal*, p1, May 23, 1989.
5. Gutis PS: New York study cites losses for two-thirds of hospitals. *New York Times* p16, June 20, 1989.
6. Hadley J, Swartz K: The impacts on hospital costs between 1980 and 1984 of hospital rate regulation, competition, and changes in health insurance coverage. *Inquiry* 1989; 26:35-47.
7. Robinson JC, Luft HS: Competition, regulation, and hospital costs, 1982 to 1986. *JAMA* 1988; 260:2676-2681.
8. Zuckerman S: Rate setting and hospital cost-containment: all-payer versus partial-payer approaches. *Health Services Research* 1987; 22:307-326.
9. Schramm CJ, Renn SC, Patrick JA, et al: A study of the cost effectiveness of medicare waivers and the efficacy of state all-payer hospital payment systems. Coalition on state all-payer hospital payment systems, Health Insurance Association of America, August, 1987.
10. Health Care Financing Administration: *Medicare Hospital Mortality Information 1987*, US Department of Health and Human Services, Washington, DC, 1988.
11. Hannon E, Hartman T: A critique of the 1987 HCFA mortality study based on New York data. State of New York Department of Health, Office of Systems Management, 1988.
12. Green J, Wintfeld N, Sharkey P, et al: The importance of severity of illness in assessing hospital mortality. *JAMA* 1990; 263:241-246.
13. Green J, Passman LJ, Wintfeld N: Analyzing hospital mortality: the consequences of diversity in patient mix. *JAMA* 1991; 265:1849-1853.
14. Park RE, Brook RH, Koseoff J, et al: Explaining variations in hospital death rates: randomness, severity of illness, quality of care. *JAMA* 1990; 264:484-490.
15. Smith DW, Pine M, Bailey RC, Jones B, et al: Using clinical variables to estimate the risk of patient mortality. *Med Care* 1991; 29:1108-1129.
16. Chu F, Cotter D, Hamilton MA: NHSPPS report on Medicare hospital mortality statistics: a detailed analysis of the mortality profile of the Northeastern states. Medical Technology and Practice Patterns Institute. Washington, DC, May, 1989.
17. Hartz AJ, Krakauer H, Kuhn EM, et al: Hospital characteristics and mortality rates. *New Eng J Med* 1989; 25:1720-1724.
18. Fink A, Yano EM, Brook RH: The condition of the literature on differences in hospital mortality. *Med Care* 1989; 27:315-336.
19. Henry JB, Lagoe RJ, Schiess WA: Mortality of medicare hospital patients in New York State, 1983-1985. *QRB*, 1988; 86-91.
20. Sager MA, Easterling DV, Kindig DA, et al: Changes in the location of death after passage of Medicare's prospective payment system. *New Eng J Med* 1989; 320:433-439.
21. Blumberg M, Binns G: Risk-adjusted 30-day mortality of fresh acute myocardial infarctions. The Hospital Research and Educational Trust, American Hospital Association, Chicago, IL, 1989; 22:307-326.
22. Manheim L, Feinglass J, Shortell S, et al: Regional variation in Medicare mortality. *Inquiry* 1992; 29:1.
23. Hahn RA, Teutsch SM, Rothenberg RB, et al: Excess deaths from nine chronic diseases in the United States, 1986. *JAMA* 1990; 264:2654-2659.

Sudden death after acute myocardial infarction

CASE PRESENTATION

Steven Goldberg, MD (Attending Physician, Division of Cardiology): A 60-year-old, white woman entered the Emergency Department of another hospital with complaints of substernal chest pressure and diaphoresis for one hour.

Over the preceding two years, she had been treated for hypertension without medication; her serum cholesterol had been 240 mg/dL. One hour before seeking medical attention, she noted the onset of substernal chest pressure, with radiation to the back and both shoulders, associated with diaphoresis. An electrocardiogram (ECG) was performed in the Emergency Department; two hours later the symptoms subsided, and she was discharged. Several hours later, the symptoms recurred; her cardiologist examined her, secured an ECG, and admitted her to the other hospital. Over the next three days, her ECG demonstrated the evolutions—all in leads V2 to V6; Q waves appeared in leads II, III, and aVF. Serum enzyme changes were compatible with an acute myocardial infarction.

During this hospitalization, the patient had recurrent episodes of chest pain; on the third hospital day, she experienced more severe pain and became hypotensive after the administration of nitroglycerin.

Joseph Ma, MD (Assistant Professor of Medicine, Cornell University Medical College): An echocardiogram performed at the other institution revealed moderate-to-severe segmental left ventricular dysfunction with akinesis of the distal $\frac{2}{3}$ of the anterior wall, septum, apex, and distal inferior wall. The anterior leaflet of the mitral valve moved toward the septum during systole, suggestive of the presence of systolic anterior motion of the mitral valve. In the apical two-chamber view, the proximal interventricular septum measured 1.5 cm in thickness and was thicker than the posterior wall, suggesting the presence of asymmetric septal hypertrophy. In the subcostal, four-chamber view, a moderate amount of pericardial effusion was evident. The continuous-wave Doppler interrogation across the aortic valve and the left ventricular outflow tract revealed a peak velocity of approximately 2.5 m/sec. In the presence of normal aortic valve opening, the increased velocity is consistent with left ventricular outflow tract obstruction at rest.

Dr Goldberg: At the other hospital, she was treated with diltiazem, heparin, aspirin, ranitidine, and a 24-hour nitroglycerin transdermal patch.

Her past medical history included a hysterectomy and oophorectomy for fibroids 15 years earlier and an episode of "gastritis" 12 years earlier, which was treated with magnesium hydroxide, aluminum hydroxide, and simethi-

cone (Mylanta). The family history was negative for cardiac diseases. The patient had smoked 2–3 packs of cigarettes per week during the preceding 30 years.

Four days after the onset of symptoms, on transfer to the North Shore University Hospital for cardiac catheterization, her physical examination revealed a blood pressure of 92/60 mm Hg, heart rate of 78/min with a regular rhythm, respiratory rate of 16/min, and a temperature of 36.7° C. The lungs were clear on auscultation. The cardiac sounds (S1 and S2) were normal, a fourth heart sound (S4) was audible, and a II/VI systolic ejection murmur was heard best along the left sternal border and was intensified by the Valsalva maneuver.

The hemoglobin was 11.9 g/dL, the hematocrit (Hct) 35.9%, the white blood cell (WBC) count 7,900/ μ L; the serum potassium level was 4.3 mmol/L, the blood urea nitrogen was 10 mg/dL, the serum creatinine was 0.8 mg/dL, the serum cholesterol was 176 mg/dL, and the cardiac enzyme levels were within normal limits. On the day of transfer, the patient underwent left and right cardiac catheterization.

Stanley Katz, MD (Chief of Cardiology): The catheterization revealed the cardiac output to be within the normal range of 5 L/min; the right atrial pressure was 11 mm Hg, the pulmonary artery systolic pressure was slightly elevated at 34 mm Hg, and the pulmonary wedge pressure 20 mm Hg. During catheterization, the systolic blood pressure was 120 mm Hg. On the angiogram, a large dyskinetic area was visible on the end-systolic frame, with very little motion in the anterior apical region; the ejection fraction was 24%.

At cardiac catheterization, there was no gradient across the aortic outflow track; the aortic systolic and left ventricular systolic pressure were equal. After a premature ventricular contraction, there was a ventricular-aortic pressure gradient of about 20–30 mm Hg; the ventricular pressure was higher than the aortic systolic pressure which decreased.

In the left ventricular angiogram, in the right anterior oblique projection, a large discrete anterior apical and inferior apical aneurysmal dyskinetic area was noted, in the distribution of the left anterior descending coronary artery. The high lateral wall and the posterior wall contracted well, and there was no mitral regurgitation.

To our surprise, injection of the left coronary artery system, including the left anterior descending, left main, circumflex, and large diagonal arteries, showed only a mild degree of atherosclerotic plaque formation but no obstruction. The right coronary artery was ectatic, with considerable plaque formation but no obstructions.

Dr Goldberg: The patient tolerated the catheterization procedure without event. Diltiazem was discontinued, and the patient was treated with verapamil. One day after transfer, in the late evening the patient experienced chest pain which was relieved by sitting forward and worsened by lying supine. A friction rub was heard, a diagnosis of

Based on a clinical conference held at North Shore University Hospital, Manhasset NY, on October 11, 1992.

Editor: JOHN T. FLYNN, MD.

Address correspondence to Dr Flynn, Consulting Editor, New York State Journal of Medicine, PO Box 5404, 420 Lakeville Road, Lake Success, NY 11042.

pericarditis was made, and treatment with ibuprofen 600 mg twice daily was begun.

On the third hospital day, the patient continued to complain of pleuritic-like chest pain; the blood pressure was 94/70 mm Hg, the pulse was 90/min, the respiratory rate was 12/min, and the temperature was 36.6° C. Aspirin was given, and coumadin therapy was begun.

On the fourth hospital day, her blood pressure was 90/56 mm Hg, with a pulse rate of 94/min, respiratory rate 20/min, and a normal temperature with enteric-coated aspirin. The WBC count was 13,000/ μ L. Verapamil, magnesium hydroxide, aluminum hydroxide, and simethicone (Mylanta) were continued, and the patient was symptomatically improved.

Later that same day, the Hg was 12.2 gm/dL, the Hct 36.5%, and the platelet count 345,000/ μ L, but the WBC count had risen to 20,000/ μ L, presumably because of the pericarditis; there was no signs of infection. Aspirin was withheld to determine if it was masking temperature elevations, and the verapamil dosage was reduced to 40 mg three times daily because of the low blood pressure.

In the late evening of the same day, after requesting a bedpan, the patient became unresponsive, and her heart rate decreased to 30/min. A cardiopulmonary code was called; resuscitation measures included a pericardial aspiration. In spite of the administration of intravenous epinephrine and dopamine, the systolic blood pressure remained below 50 mm Hg; she experienced ventricular tachycardia and later ventricular fibrillation which could not be interrupted by several attempts at cardioversion. The patient was pronounced dead at 10:30 PM on the fourth hospital day.

I would like to highlight several aspects of this patient's initial presentation and several interesting points in the differential diagnosis, some of which are already obvious from the echocardiograms and angiograms.

Initially, at the other hospital her ECGs showed normal sinus rhythm. I believe that the Q waves in leads II, III, and aVF were already present before the marked antero-septal and antero-lateral ST segment elevations occurring on day one and day two at the other hospital. During that period, she also developed terminal T-wave inversions and inferior changes as well. All these changes point to an evolving anterior apical myocardial infarction.

After transfer to our hospital, the T-wave inversions appeared less prominent, although the ST elevations became more so. These changes suggest either an aneurysm or pericardial inflammation. One day later, the ST elevations became more pronounced and more diffuse, at a time when the patient had a pericardial effusion and pleuritic positional chest pain. Some of these ST elevations perhaps represent a degree of pericarditis, about which it is impossible to be certain, in view of the ECG changes caused by the infarction. However, in fact, we do observe before death these diffuse ST elevations, the earlier Q-waves in the inferior leads, and some terminal T-wave inversions in leads V2 and V3 which were present earlier as well.

My discussion is guided by my commitment to the importance of physical diagnostic signs. On presentation at our hospital, a systolic murmur was noted. An appropriate differential diagnosis of systolic murmurs is fundamental to physical diagnosis, but is not always a straightforward exercise. In the presence of an acute myocardial infarction, certain special considerations may or may not be relevant to the diagnosis of hypertrophic cardiomyopathy.

A holosystolic murmur present at the apex might represent evidence of mitral insufficiency, or tricuspid insufficiency if it is located more toward the right sternal border, or even a ventricular septal defect (VSD). With VSD associated with a myocardial infarction, however, the murmur would usually be loud and associated with hemodynamic compromise and often with a thrill.

The differentiation among these murmurs may require the use of aids to auscultation at the bedside, which we probably do not use as much as we should.¹ I wish to spend a few moments on the differentiation of various systolic murmurs: right-sided and left-sided, as well as flow-type murmurs across the aortic valve in contrast with regurgitant murmurs across the mitral valve.

Among the available respiratory variants during the physical exam, we can try the Corvalto maneuver, that is, asking the patient to take a deep breath. This results in a reduction of pressure within the thoracic cavity and increases the blood flow across the right side of the heart immediately. If there is a tricuspid murmur, the Corvalto maneuver will tend to increase its intensity. This can occur with acute myocardial infarction, which may contribute to right ventricular dysfunction and right ventricular failure.

Similarly, the Mueller's maneuver, that is, a forceful inhalation against a closed glottis, decreases the intrathoracic pressure and will increase the venous return to the heart and may increase a right-sided murmur.

The classic Valsalva maneuver may be helpful in differentiating the nature of a systolic murmur. During the early strain phase, the flow to the right and left sides of the heart is reduced and the loudness of a regurgitant murmur may be reduced; the flow across a stenotic aortic valve may also be reduced. However, by reducing the flow and dimensions within the left ventricle, the early strain phase of the Valsalva maneuver will increase the dynamic pressure gradient from left ventricle to aorta, thus increasing the intensity of the murmur of aortic stenosis. Similarly, if the patient has significant idiopathic hypertrophic subaortic stenosis (IHSS), we may expect the ejection murmur to become louder, as was described on the physical examination of this patient.

Squatting directly increases venous return to the heart and increases ventricular diameter, so that in the dynamic situation of a changing gradient across the subaortic area in IHSS, the increased flow from squatting will reduce the intensity of the murmur. After auscultating the heart while the patient is squatting, if you continue to auscultate as you stand up with the patient, the immediate and dramatic reduction in the volume within the ventricular cavity can cause the IHSS murmur to increase in intensity. Other murmurs may be little changed by this maneuver, although it may lead to a decrease in the murmur of mitral insufficiency because of the reduced flow within the ventricular chamber.

Hand grip can be a helpful maneuver, although you must make sure that when you urge the patient to tighten his grip, he does not also involuntarily perform the Valsalva maneuver. A pure hand grip will increase peripheral vascular resistance, which in turn tends to reduce the pressure gradient between left ventricle and aorta, and thus tends to reduce the intensity of the systolic murmur in IHSS.

An interesting observation on this patient in the catheterization laboratory was the increased intensity of the systolic murmur immediately after a premature ventricular contrac-

tion (PVC). This would be compatible with IHSS, since during the compensatory pause after a PVC the ventricle has an opportunity to become hyperdynamic. The increased contractility of the beat immediately after the PVC will often cause the murmur to become louder in IHSS, since the minimal or moderate pressure gradient between ventricle and aorta can thus become more significant. This additional fact tends to support the diagnosis of IHSS in this patient.

Artificial intensification of a murmur can result from the administration of an inotropic agent such as isoproterenol, which tends to increase the pressure gradient in IHSS.

The differential diagnosis of the causes of a murmur in a patient experiencing an acute myocardial infarction should include a VSD. When this results from infarction and septal rupture, it can produce a loud murmur at the left lower sternal border together with a thrill; hemodynamic compromise may also be evident. During right-heart catheterization, one may see a step-up in blood oxygenation, when a Swan Ganz catheter is passed from the right atrium to the right ventricle and then into the pulmonary artery. Increased blood oxygenation will be discovered where it should not occur, because of oxygenated blood passing from left to right ventricle through the VSD. Similarly, a color Doppler echocardiogram may easily confirm the presence of a VSD.

In the presence of a myocardial infarction, a new murmur may also reflect disruption of papillary muscles of the left ventricle. The posteromedial papillary muscle especially may be damaged in infarctions of the inferior and posterior wall, where the circumflex and right coronary artery have a preponderance of flow. Part of the papillary muscle may rupture, but rarely will it rupture completely and cause acute mitral insufficiency. In this latter circumstance, however, a new, low systolic murmur can develop, most often with radiation into the axilla, and often associated with acute disastrous hemodynamic compromise. Hypotension and pulmonary edema can result. This train of events, however, differs from the sudden death which this patient experienced.

We are told of a systolic murmur at the base of the heart in this patient, but no mention is made of a carotid pulse tracing; a diminished and delayed carotid pulse tracing, that is, *pulsus tardus et parvus*, would lead us to suspect the presence of aortic stenosis. In this case, also, there is no description of a thrill, which can occur with aortic stenosis or VSD or mitral insufficiency.

In evaluating a systolic murmur in the office or at the bedside, we face the classic dilemma as to which patient truly deserves an echocardiogram to differentiate aortic stenosis from IHSS. In which patient should we be seriously concerned about the risk of sudden death? Would not the carotid tracing show a difference, with a double peak, as seen in IHSS, versus the delayed and slow peak of aortic stenosis? An S4 gallop is often heard with the stiff ventricle of both aortic stenosis and IHSS.

The normal physiological splitting of the second heart sound (S2) involves delay in the closure of the pulmonic valve with inspiration. However with significant aortic stenosis, the aortic valve closes late, so that with inspiration the closure of the pulmonic valve overtakes the closure of the aortic valve. Thus, the two valve sounds move closer together with inspiration and further apart with expiration. This so-called paradoxical splitting of the second heart sound was not commented on in this patient; in fact, the

second sound is described as normal. In IHSS, paradoxical splitting of the S2 can be heard with a significant pressure gradient, whereas in this patient the gradient was insignificant. However, the ventricular-aortic pressure gradient increased and the intensity of the murmur increased in this patient with the Valsalva maneuver. If we were to give a patient with IHSS isoproterenol and thus increase the ventricular contractility, a previous minimal pressure gradient at rest would increase, and an almost normal carotid pulse contour could change to a marked spiked dome appearance, that is, the double pulse of IHSS.

The murmur in this patient, in my judgment, represents primarily a systolic murmur increased by the Valsalva maneuver, and corresponds to the documented findings on echocardiogram and on cardiac catheterization, supporting a diagnosis of hypertrophic cardiomyopathy. However, that diagnosis does not always imply an obstructive cardiomyopathy. In most recent medical terminology, it would be termed hypertrophic cardiomyopathy.

As her course progressed, the patient again experienced recurrent chest pain, some of which was no doubt due to myocardial infarction. We know that she had a pericardial effusion and her later pain differed from her earlier infarction pain, since it was characterized as positional in nature with radiation to the scapular area. A patient like this who develops angina two or three days after an infarction raises the question as to whether an emergency cardiac catheterization is indicated.

Or is the pain due to pericarditis, which pathologically may be present in a third or more of cases of infarction? Clinically, you might hear a pericardial rub in 10% or so of patients with myocardial infarction. How are we going to distinguish between post-infarction ischemic pain and pericarditis as the cause of the pain?

The most important element in the diagnosis, as in all of medicine, is an accurate history. Are the symptoms that of a pressure pain, is it constrictive in nature, does it radiate to the neck and left arm which is more typical of angina, or is it a bit more atypical? Is it a sharp pain, is it positional, is it eased when the patient sits up, does it radiate more to the scapular area? The duration of the pain can be important, whereas angina may last for minutes, pericardial pain may last for hours.

Sometimes the distinction between acute pericarditis and chronic Dressler's pericarditis is not quite clear. In Dressler's pericarditis, that is, the later post-infarct pericarditis, the pain may last weeks, months, or sometimes years. The effects of respiration should be determined. The pain of pericarditis is more often pleuritic in character and is intensified by respiration, as opposed to the lack of respiratory change in pain caused by myocardial infarction or ischemia.

The classic helpful finding in pericarditis would of course be a friction rub—a one-two-three component rub representing the movement of the atrium and ventricle in systole and the relaxation of the ventricle in systole, as well as the relaxation of the ventricle in early diastole. However, these three components of the friction rub may not all be present. Sometimes if only one component of a friction rub is present, it may not be so easy to distinguish it from a short murmur. However, the leathery-friction quality of the rub frequently forms the basis of our differentiation of it from a murmur.

In the ECG in pericarditis, we might expect more typically to observe the upward concave appearance of the

ST-segment and T wave, in contrast to the more dome-like appearance with an infarct. In addition, depression of the PR interval might be expected to be seen in pericarditis; such changes are very difficult and unusual to find in the setting of an infarct especially when it has caused such diffuse ECG changes as in this patient.

At the catheterization of this patient, the physician was very surprised to find that the patient had "clean" coronary arteries. Only a very small percentage of patients with myocardial infarction demonstrate such a finding. An extensive differential diagnosis applies to patients who experience myocardial infarction in the presence of normal-appearing or nearly normal-appearing coronary arteries.

We must ask ourselves if this is truly an instance of clean coronary arteries, since there is mention of plaque formation within the vessels. The patient was a heavy smoker, was hypertensive, and had moderate hypercholesterolemia. So it is not a total surprise that she should have some degree of atherosclerosis. In fact, however, approximately 6% of myocardial infarcts occur in a setting of minimal to not-so-obvious atherosclerosis on angiography.

Since the classic studies of DeWood in 1980,² we know that coronary thrombosis is almost always involved with the acute infarct, but that thrombosis does not always occur at a point of maximal atherosclerotic obstruction. If you follow patients with three-vessel disease in whom the lesions vary from 50% to 90% in different coronary arteries, you find it impossible to predict where the thrombosis and the resulting infarct are going to occur. It might as well occur at the site of 50%-60% stenosis as at the 90% stenosis. We now know that the tone of the blood vessel is important in this regard.

In this patient, were there elements of coronary spasm that occurred, or of plaques that suddenly ruptured, or of thromboses that occurred because of a hematological abnormality or of a hypercoagulable state? Was there evidence of a rheumatologic process that could contribute to coronary thrombosis in a patient without significant atherosclerosis? Was there endocarditis with coronary embolism or were there the side effects of earlier radiation therapy causing advanced atherosclerosis? Could there be a dissection of the aorta involving the coronary arteries as well? In a child, could coronary thrombosis and myocardial infarction be secondary to Kawasaki disease?

The differential diagnosis of embolic events and infarction in the setting of minimal coronary artery disease is very long. If this patient had IHSS, there could be a blood supply-oxygen demand mismatch. In severe aortic stenosis and in advanced hypertrophic cardiomyopathy, the demands of the extremely hypertrophied ventricle may outstrip the coronary blood supply even with minimal coronary disease. In aortic stenosis, the risk of sudden death and its cause are usually not related to coronary disease, but to the blood supply-metabolic demand mismatch. If the patient in this setting has prolonged hypotension where the demands cannot be met even in the absence of atherosclerosis, such an event can lead to infarction.

One interesting point here: This patient did not receive thrombolytic therapy. There is debate as to the timing and selection of patients for thrombolytic therapy. This patient did not present in a hyperacute situation, and the minimal ECG changes also did not support an urgent need for thrombolytic therapy. However, should thrombolytic agents be given to a patient with so-called "clean" coronary arteries or to a cocaine abuser or to a patient with coronary

vasospasm? Most often, there probably is a decent rationale to give the therapy because even with minimal plaque formation the patient may still be in a hyperacute situation in which spasm could be the initiating factor leading to thrombosis and eventual infarction. So thrombolytic agents may play a role in the hyperacute situation, even with "clean" coronary arteries.

This patient received coumadin toward the end of her hospitalization, and before that had a moderate pericardial effusion. Several years ago, many clinicians were opposed to anticoagulation in such a situation. Most recent data has suggested that post-infarction pericarditis, even with a small pericardial effusion, poses a very small risk of progressing to the point of tamponade in the presence of anticoagulation.³ Even with a small pericardial effusion, if there is sufficient indication for anticoagulation, it can be done carefully.

This patient died suddenly after a massive myocardial infarction with the development of a large ventricular aneurysm. An aneurysm may be due to an initial local hemorrhage within the myocardium that may form a local diverticulum, that can extend to the epicardium. Eventually as the connective tissue spreads apart, there may be eventual rupture of the muscle. Such an event is the most common cause of the sudden witnessed cardiac arrest, such as occurred in this patient. This aneurysm, present earlier, was apparently a true aneurysm, in the formation of which the wall thins and expands and sometimes forms a sacculi. In this patient, the myocardial infarct was so massive that she formed a diffuse aneurysm of the left ventricle.

Sometimes a false aneurysm may appear, lined not by heart muscle but by pericardium only. That might have been a strong likelihood in this patient; the formation of a false aneurysm may afford an extra margin of time in which to consider surgical intervention.

The patient, therefore, in view of the sudden circumstances of her death, and the fact that she had had such a massive aneurysm, most likely experienced ventricular rupture. This complication is relatively uncommon, causing 10%-15% of deaths in the coronary care unit. Such a rupture through the ventricle will involve the free wall in 85% of cases, and only a smaller number, perhaps 5%, will involve the papillary muscles. Approximately 10% involve the interventricular septum with an acute VSD.

Finally, let me briefly discuss the hypertrophic cardiomyopathy, which is apparently a side issue here. It may be a bit of a red herring in this case. The hypertrophic cardiomyopathy does not appear to have been severe; in the catheterization laboratory, there was virtually no pressure gradient between ventricle and aorta. Three days earlier, in the echo laboratory at the other hospital, a very modest gradient was described. The gradient can vary with time, but in her case at no point was it severe.

I don't think that this was an instance of blood supply-oxygen demand mismatch which would be more typical of severe hypertrophic cardiomyopathy. This patient was asymptomatic before the infarction, without the dyspnea, occurring 90% or more of the time in hypertrophic cardiomyopathy. There was no earlier angina pectoris, no history of arrhythmias, and no past awareness on the part of the patient of a heart murmur, at least according to the Clinical Pathological Conference protocol.

This seems to be a case of mild hypertrophic cardiomyopathy, as is more frequently seen in the physician's office. Our pathologist may present only some swirls of disarray

among the myocardial fibers within the myocardium. Pathophysiologically, the pressure gradient referred to here resulted from the septal thickening and partial obstruction to the ventricular outflow toward the aortic root, as the anterior leaflet of the mitral valve during systole bends and bows toward the aortic root and interferes with the outflow. This systolic anterior motion (SAM) during systole leads to a pressure gradient; if the left ventricular chamber becomes smaller in volume because the patient is dehydrated or because of the Valsalva maneuver, the gradient becomes worse. The gradient is a dynamic situation.

As I indicated, clinically the patient did not have early symptoms which one might expect with hypertrophic cardiomyopathy: dyspnea, chest pain, syncope, or dangerous ventricular arrhythmias at times. Her ECG, however, on presentation showed small Q waves in leads II, III, and aVF, with no obvious or documented earlier inferior wall infarction; such ECG findings perhaps may reflect changes due to hypertrophic cardiomyopathy. However, electrocardiographically we would expect to see more evidence of severe hypertrophy, with very tall R waves in the lateral leads and T waves inverted anterolaterally, especially in a patient with no overt hypertension or even with minimal hypertension. With hypertrophic cardiomyopathy, a very obvious hypertensive pattern on the ECG with very dramatic voltage, and T-wave inversions are sometimes associated with accessory atrioventricular conduction pathways, short PR intervals, and δ -waves.

I propose that the patient's baseline ECG, which suggests a possible inferior wall infarction does not represent an inferior infarct but rather changes due to her hypertrophic cardiomyopathy.

In summary, we are discussing a lady with hypertrophic cardiomyopathy, which had a minimal relationship to her current condition. She had minimal plaquing of her so-called "clean" coronary arteries that were probably and unfortunately subject to vasospasm and temporary thrombosis, with spontaneous recanalization without thrombolytic therapy. These events lead to a disastrously large anteroapical infarct, the size of which was increased by the lack of collateral circulation to nourish the anterior wall when the coronary artery was occluded. The result was the rapid appearance of a large aneurysm of the entire anteroapical wall, which four days post-infarction led to a rupture of the free wall of the left ventricle.

CLINICAL DIAGNOSIS:

Acute antero-apical myocardial infarction, with pericarditis.

Mild hypertrophic cardiomyopathy.

Acute myocardial free-wall rupture as cause of sudden death.

PATHOLOGY PRESENTATION

Ellen Kahn, MD (Attending Pathologist, NSUH: Associate Attending, Department of Pediatrics, NSUH: Professor of Clinical Pathology, Cornell University Medical College): I wish to present the pathological findings, some of which correlate positively and closely with the clinical facts, whereas others diverge from the clinical observations.

The patient presented initially on hospital day 1 with chest pain; on day 4 with a pericardial friction rub; and on day 6 with abrupt cardiac arrest. The most dramatic finding at autopsy consisted of a large blood clot weighing 200 g and occupying the pericardial cavity, associated with a

considerable amount of fluid blood. The heart itself was mildly enlarged, weighing 400 g and presented an area of roughening of the epicardium corresponding to pericarditis. A probe could be passed through an area of ventricular rupture in the lateral wall of the left ventricle, where the initial infarction had been associated with focal hemorrhage and myocardial rupture (Fig 1).

Histologically, the area of infarction was characterized by a bright pink appearance, with necrotic myocardial fibers and at the periphery a large amount of fibrous connective tissue (Fig 2). Fibroblasts and macrophages appear in an area of myocardial infarction on day 5, so that the age of this infarct is at least six days, if not older. The infarct was transmural, involved the anterior wall and the lateral wall, and was complicated by a small mural thrombus and by pericarditis with fibrinous organizing exudate. This latter inflammation was therefore at least several days old.

Areas of waviness of the myocardial fibers are indicative of extension of the infarct; focal areas of drop-out throughout the myocardium indicate diffuse damage probably occurring during the initial phase of the myocardial infarction. Of note was the absence of any large scar, indicative of antecedent infarction.

The left ventricular cavity was the site of a simple track, the site of hemorrhagic necrosis of the myocardium, as seen under higher power. We should keep this pattern in mind when we discuss the pathogenesis of the myocardial rupture.

Although not of obliterative character, I would not classify the coronary arteriosclerotic disease in this patient as mild. The right coronary system showed marked intimal thickening and reduction of the lumen by 80%–85%. The finding was by no means diffuse but was multifocal and present, to a lesser degree, in the left and circumflex coronary arteries, as well.

We did not find evidence of ventricular aneurysmal dilatation. In the area of the myocardial infarction, there was not the thinning of the ventricular wall that had been predicted. Moreover, the wall thickness of the interventricular septum was not disproportionate to that of the posterior wall of the left ventricle. At autopsy, the interventricular septum measured 1 cm and the posterior wall of the left ventricle measured 1.4 cm. The ratio of the interventric-

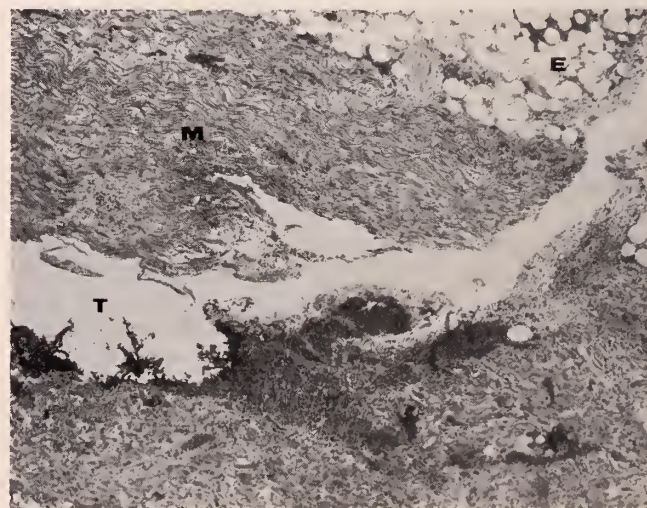


FIGURE 1. Area of myocardial perforation, with simple track (T) associated with hemorrhage. (M) myocardium; (E) epicardium (Hematoxylin-eosin stain; original magnification $\times 40$).

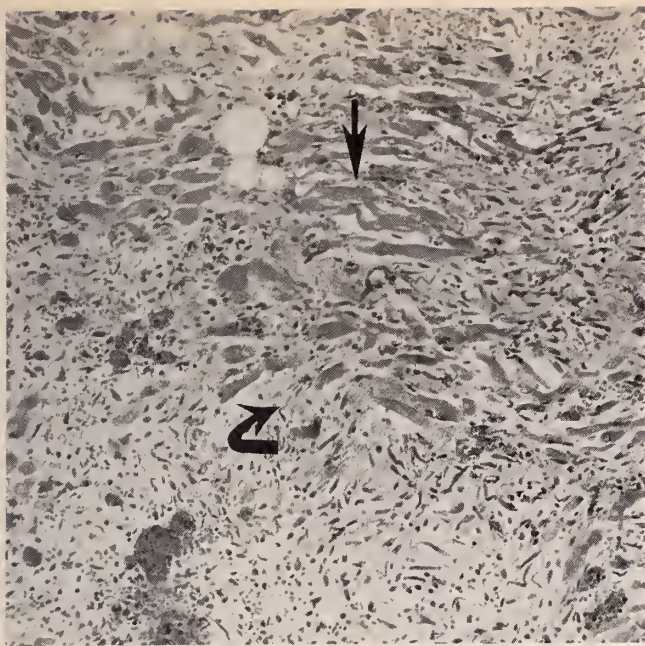


FIGURE 2. Area of myocardial infarction, with necrotic muscle fibers (at straight arrow) associated with fibroblastic proliferation (at curved arrow) (Hematoxylin-eosin stain, original magnification $\times 200$).

ular septum over the posterior wall of the left ventricle of 0.7 is not consistent with the diagnosis of asymmetrical septal hypertrophy.

If you are still a disbeliever, then the microscopic examination should convince you, since there was no disarray of muscle fibers in the sections taken from the interventricular septum.

How then can we correlate the pathologic findings that were genuine with the reported clinical findings? In a report concerning the dynamics of left-outflow tract obstruction in the absence of a cardiomyopathy,⁴ the patient who was described developed a gradient between the aortic and left ventricular systolic pressure in the presence of a hemopericardium. However, the changes in hemodynamics in our patient preceded the hemopericardium, which therefore cannot be blamed for the changes. In other anecdotal cases, outflow tract gradients were found, in the setting of a myocardial infarction and in the absence of a hemopericardium. Such dynamic changes were due, according to the authors, to a combination of increased contractility plus decreased left ventricular function. These could be attributable to a hemopericardium, when present, or to dyskinesia or akinesia.

The remaining findings in our case were consequences of the myocardial infarction: bilateral pleural effusions, acute passive congestion of the lungs with vascular congestion, and minimal evidence of chronic passive congestion with hemosiderin-laden macrophages. There was evidence of shock with ischemic necrosis of the liver. An adenoma of the parathyroid was present but appeared to be non-functional. The spleen showed isolated necrotizing granulomata that were also present in the lymph nodes at the hila of the lungs and in the mesentery. No micro-organisms were detected by special stains.

The schema of events here involved arteriosclerosis of the coronary arteries, myocardial infarction, complicated by pericarditis and ventricular rupture, hemopericardium leading to shock with resulting hepatic necrosis and death.

Rupture of the ventricular wall occurs most often after 60 years of age, predominantly in female patients in that age group; before age 60, males predominate. Hypertension is a risk factor; absence of left ventricular hypertrophy is common. In a series of 100 autopsied patients in whom 98% had critical coronary atherosclerotic disease, rupture most often followed the first myocardial infarction.⁵ The incidence of rupture seems to have been stable over the years.

Rupture involves the left ventricle more frequently than the septum and papillary muscles; it occurs in the mid-ventricular portion and usually the lateral wall. If the infarct is located in the basal or middle portion of the ventricle, a lateral perforation is more likely; an infarct in the apical area leads predominantly to an anterior rupture. However, in the majority of the cases, the site of rupture seems to be in the mid and lateral portions of the left ventricle.

Myocardial rupture appears to have a seasonal occurrence, most often in the fall and the spring; quite frequently ventricular rupture is silent. It is most likely to occur in the latter half of the first week after the infarct, although it can occur both before and after that period of time. This negates the idea that the rupture is most likely to occur when the myocardium is at its weakest, when there is polymorphonuclear cellular infiltrate, myocardial softening, and destruction on Days Four and Five.

When a rupture occurs on Day One of a myocardial infarction, other factors must be involved. There may be increased stress secondary to contraction of two adjacent papillary muscles, which would explain a rupture in the mid-portion of the lateral wall where the papillary muscle inserts. It would also explain why the rupture occurs between the affected and unaffected portions of the myocardium where the shear forces are more intense. Perhaps other factors intervene, such as intramyocardial hemorrhage associated with anticoagulation or perhaps with coronary artery revascularization. Finally, there is some suggestion, although not proven, that non-steroidal anti-inflammatory agents may play a role in ventricular rupture.⁶

In summary, I described to you a 60-year-old female patient who presented initially with acute myocardial infarction, in the setting of critical coronary atherosclerosis, complicated by fibrinous pericarditis, and who on day 6 developed a classic perforation, that is, of the left ventricle, mid-portion, lateral wall.

Dr Goldberg: Perhaps because so much of the distal, anterior, and lateral walls of the left ventricle were hypokinetic or akinetic, the proximal septum was relatively hyperdynamic, and this imbalance led to the minor degree of dynamic outflow obstruction and the echocardiographic and catheterization findings.

Dr Meyer: So you suggest that the proximal septum was not truly hyperdynamic, but rather that the rest of the ventricular wall was so hypodynamic?

Dr Goldberg: In the face of the sympathetic storm from the infarct, the very proximal septum was "hyper," whereas the rest was not. The upper lateral wall was still intact and there may have been a temporary physiologic obstruction at that point. The other question is, was the uppermost portion of the septum thickened at all? Dr Kahn indicates that such was not the case.

Dr Ma: It was interesting that the proximal septal thickness was found to be normal at autopsy even though the proximal septum appears to be thickened on the

echocardiogram. Nevertheless, obstruction to left ventricular outflow can still be produced by the combination of SAM motion of the mitral valve and a septum that is sigmoidal in shape, in a patient without hypertrophic cardiomyopathy.

Dr Katz: For a long time, we have been aware of discrepancies between what angiographers find in the coronary arteries on angiogram and what the pathologists find at autopsy. My impression of the angiogram is that it certainly indicated coronary artery disease but not the discrete obstruction that we usually see in most of the infarction patients that we study. What I am implying is that there is no obstruction to account for the infarct.

My second observation is that angiographers disagree with everybody about ventricular aneurysms. We frequently diagnose an aneurysm on the ventriculogram and refer the patient to the cardiac surgeon who does not find an aneurysm at operation. So we try to hedge by referring to aneurysmal dilatation, implying that it is not quite an aneurysm, but that a portion of the ventricle is dilated beyond the diastolic silhouette that you would expect to see.

On this patient's angiogram, there was certainly aneurysmal dilatation in diastole; the diastolic silhouette extended well beyond what you would normally expect. However, diagnosis of an aneurysm on an angiogram is not always very accurate.

Marvin E. Cramer, MD (Attending Cardiologist): Why can't both the angiographer and the surgeon or the pathologist be correct? In the autopsy room and in the operating room with the thoracic cage opened, the negative pressure which is normally within the thoracic cage is absent; whereas in the catheterization laboratory and during injection of the coronary arteries and the ventricles, that negative intrathoracic pressure is present. So the angiographer is observing the ventricle surrounded by the normal negative pressure within the chest.

In addition, there is a positive pressure within the ventricle especially during systole which you, the angiographer, are observing but which is not seen in the morgue nor in the surgical condition when the heart is bypassed by the perfusion pump. This combination of pressure differences could contribute under ordinary circumstances to a ballooning out of a weakened ventricular wall and create for the angiographer the impression of an aneurysm. Could that be the reason for the discrepancy?

Dr Katz: The pathologists and the surgeons have differing criteria for the diagnosis of ventricular aneurysm. In the operating room, you need to find a discrete area of myocardial thinning which actually collapses when the heart is decompressed and arrested during bypass. Then, the surgeon has a distinct area which he can resect.

Another interesting observation is that patients whom we restudy by angiography after ventricular aneurysmectomy still present to us the appearance of an aneurysm. It is as though the surgeon had done nothing. From the pathologist's presentation, you can see from the sections that there was certainly no thinning of the ventricular wall. It showed the same thickness all the way around, even at the apex, whereas the angiogram indicated an aneurysm.

In terms of the coronary arteries, it is true that the pathology sections are secured on decompressed arteries so that you can't really be sure as to the diameter of their lumens during life. However, you did see the presence of intimal atheroma. The angiogram demonstrated a great

deal of atherosclerosis in the right coronary artery with a large ectatic artery but no truly obstructive disease.

Animal studies of ventricular remodelling indicate that when the pressure in the ventricle is reduced in the peri-infarction and early post-infarction period over a long time, the so-called remodelling of the left ventricle is interfered with. The cardiologist's aim is prevention of a patient's progression into a myopathic state during the first two or three years after a myocardial infarction and ultimately into congestive heart failure. A very large collaborative study, the SAVE Study,^{7,8} is ongoing at the moment, the results of which are not yet assembled. This study has enrolled patients with a systolic ejection fraction under 40%; at the time of myocardial infarction they are given either placebo or an angiotensin-converting inhibitor if their blood pressures tolerate it. These patients will then be followed for several years to see if the individuals who were given ACE inhibitors have less frequent congestive heart failure than those patients who were given placebos. However some physicians have anticipated the results and in certain institutions it is the practice to give ACE inhibitors to patients with large, anterior-wall myocardial infarctions, especially if studies have indicated that the ejection fraction is less than 40%.

Jack M. Rubenstein, MD (Associate Attending in Medicine, Clinical Assistant Professor of Medicine, Cornell University Medical College): In the past, we would have been very concerned about anticoagulating with coumadin a post-infarct patient with pericarditis for fear of causing bleeding. Do you think that this is an issue? Were we overly aggressive in giving both anti-inflammatory and anticoagulant drugs to this patient?

Dr Katz: Coumadin was started primarily because of the large anterior wall infarct, in an effort to prevent thrombus formation in the aneurysm and subsequent embolization. The anti-inflammatory drug was started because of the patient's distressing pericardial pain, causing discomfort to the point where aspirin was added in addition to the ibuprofen. I don't think that the treatment was overly aggressive, but rather that it was appropriate. Dr Goldberg, would you care to comment?

Dr Goldberg: I had an opportunity to review the medical literature of pericarditis over the past few days; the Cardiology Clinics recently^{3,9} presented a review of pericarditis associated with large infarcts and how to treat them. There was no exact answer and there was still a theoretical concern. Dr Kahn mentioned the interference with healing processes, resulting from the use of non-steroidals when the patient's condition is acute. The information is not sufficiently solid at this point to recommend the avoidance of non-steroidal anti-inflammatory agents. There is perhaps a theoretical benefit of using high-dose aspirin, rather than ibuprofen or indocin. That is as much as anyone can comment on.

In terms of coumadin itself, certainly it is too soon to say that that played a role in the ventricular rupture in this case. In relation to the use of anticoagulation in this situation, the long-term risk of embolism from a massive anteroinfarct, I think, outweighed the acute risk of rupture.

FINAL ANATOMIC DIAGNOSIS

Cardiovascular atherosclerosis, moderate.

Coronary arteriosclerosis, three-vessel disease, grade IV.

Recent transmural myocardial infarction, anterior and lateral wall of left ventricular, with physiologic repair.

Fibrinous pericarditis with repair.

Mural thrombus of endocardium, left ventricle.
 Free rupture, lateral wall of left ventricle, with hemopericardium.
 Ischemic necrosis of the liver.
 Acute and chronic passive congestion of lungs and abdominal viscera.
 Pleural effusions, bilateral.
 Diverticulosis of rectosigmoid.
 Necrotizing granulomata of the spleen and of the periaortic and pulmonary hilar lymph nodes.
 Hypertensive cardiovascular disease, by history.

REFERENCES

1. Rothman A, Goldberger AL: Aids to cardiac auscultation. *Ann Int Med* 1983; 99:346-353.
2. DeWood MA, Spores J, Notske R, et al: Prevalance of total coronary

occlusion during the early hours of transmural myocardial infarction. *N Engl J Med* 1980; 303:897-902.

3. Gregoratos G: Pericardial involvement in acute myocardial infarction. *Cardiol Clin* 1990; 8:601-608.

4. Deligonul U, Uppstrom E, Penick D, et al: Dynamic left ventricular outflow tract obstruction induced by pericardial tamponade during acute anterior myocardial infarction. *Am Heart J* 1991; 121:190-194.

5. Batts KP, Ackermann DM, Edwards WD: Postinfarction rupture of the left ventricular free wall: clinicopathologic correlates in 100 consecutive autopsy cases. *Hum Pathol* 1990; 21:530-535.

6. Reddy SG, Roberts WC: Frequency of rupture of the left ventricular free wall or ventricular septum among necropsy cases of fatal acute myocardial infarction since the introduction of coronary care units. *Am J Cardiol* 1989; 63: 906-911.

7. Moya LA, Pfeffer MA, Braunwald E: Rationale, design and baseline characteristics of the survival and ventricular enlargement trial. *Am J Cardiol* 1991; 68:70D-79D.

8. Pfeffer MA, Moya LA, Braunwald E, et al: Selection bias in the use of thrombolytic therapy in acute myocardial infarction. *JAMA* 1991; 266:528-532.

9. Cercek B, Shah PK: Complicated acute myocardial infarction. *Cardiol Clin* 1991; 9:569-593.

White House Fellowships

The White House Fellowships were established in 1964 to provide outstanding Americans with first hand experience in the practices of governing the nation and with a sense of personal involvement in the leadership of society. Any US citizen with the exception of civilian federal government employees may apply. The duration of the fellowship is one year.

Applications are available from the President's Commission on White House Fellowships, 712 Jackson Place, NW, Washington, DC 20503.

Ethical and social issues in organ procurement for transplantation

FRED ROSNER, MD; JOHN B. HENRY, MD; JONATHAN R. WOLPAW, MD; PETER P. SORDILLO, MD, PhD; PHILIP H. SECHZER, MD; PETER ROGATZ, MD; HERMAN M. RISEMBERG, MD; FERNANDO V. ONA, MD; PATRICIA J. NUMANN, MD; ROBERT E. LOWENSTEIN, MD, PhD; LAURENCE LOEB, MD; ALLISON B. LANDOLT, MD; PIETER R. KARK, MD; ABRAHAM L. HALPERN, MD; PETER B. FARNSWORTH, MD; ERIC J. CASSELL, MD; ANTHONY BUSCAGLIA, MD; ALLEN J. BENNETT, MD

The Surgeon General of the United States recently stated that the field of transplantation has experienced an explosion of innovative technology and life-saving procedures since the first kidney transplant was performed in 1954 between identical twins.¹ Advances in organ preservation/transport techniques, immunosuppressive therapies, tissue (human lymphocyte antigen) typing, donor procurement, diagnosis, treatment, and optimal organ allocation through computers/networks have moved clinical transplantation from the experimental arena to center stage as first-line therapy for many forms of end-stage organ disease or failure.

In December 1967, the first human-to-human heart transplant was carried out, followed the next year by 102 heart transplants performed by 64 surgical teams in 22 centers around the world, with generally disastrous results.² Over the next 20 years, clinical cardiac transplantation evolved from an experimental procedure to an accepted therapeutic option for patients with end-stage heart failure.³ It is a safe and effective treatment and is measured, nowadays, not only by patient survival, but also by the quality of life achieved by those who receive this treatment.⁴

Long-term results of cardiac transplantation from Stanford University indicate that 83% of 389 patients operated on between 1981 and 1990 are alive and well one year after the procedure and that 63% are alive and well five years later.⁵ Stanford has 25 patients who have survived more than ten-years post transplant. In the 1988 official report of the International Society for Heart Transplantation (ISHT), the actuarial ten-year survival after cardiac transplantation was 73%.⁶ The ISHT also reports a 61% one-year survival rate for combined heart-lung transplantation.⁷

Liver transplantation has also come of age and "acceptable survival results have moved the procedure from the experimental area to a truly therapeutic modality" for some patients.⁸ Five-year survival rates of approximately 60% are being reported from experienced transplant centers, particularly if the liver transplant is performed for a benign rather than malignant disease. The current and future

status of kidney transplantation has recently been summarized. More than 80% of patients who undergo this procedure survive for five years and more.⁹

THE PROBLEM OF ORGAN SHORTAGE

Because of the increasing successes in organ transplantation, much recent attention has been and continues to be focused on the shortfall in the supply of donor organs. In addition, more kinds of organs are being transplanted such as pancreas, lungs, intestine, multiple organs (eg, heart/lung and kidney/pancreas) and fetal tissues. Other reasons for the increased demand for organs include the increased number of centers doing organ transplants and the expanded criteria for determining recipient eligibility.¹⁰

The need for organs is enormous. Over 60,000 people die annually or are maintained on suboptimal therapy who potentially could benefit from a kidney, heart, liver, heart/lung, pancreas, or lung transplantation.¹¹

In spite of intensive efforts and major initiatives to increase the supply of organs between 1986 and 1989, the number of donors available annually remained virtually unchanged. According to some investigators, it may be possible to increase by 80% the number of donors available in the United States since many more organ donors are available than are being accessed through existing procurement efforts.¹¹ A recent study indicates that waiting times for cadaveric kidney transplants are significantly shorter for patients younger than 15 years *v* those aged 15 through 44 years, for patients listed at multiple centers *v* one center, and for white *v* black patients.¹² Other immunologic, demographic, and technical factors also play a role. Many organizations are actively addressing both the issue of organ shortage and the equitable and just distribution of organs once they are procured. Some of these efforts are described below.

THE SELLING OF ORGANS

The organ shortage has led to the rise of commercial traffic in human organs, particularly from living donors who are unrelated to recipients. There is clear evidence of such traffic in recent years.¹³ One report describes 130 patients from three renal units in the United Arab Emirates and Oman who went, of their own accord, to Bombay where they bought, through brokers, kidneys from living unrelated Indian donors for 2,600 to 3,300 US dollars.¹⁴ Another

Address correspondence to Dr Rosner, Director, Department of Medicine, Queens Hospital Center Affiliation of the Long Island Jewish Medical Center, 82-68, 164th St, Jamaica, NY 11432.

Prepared as an educational and informational report by the Committee on Bioethical Issues of the Medical Society of the State of New York.

report describes 14 patients from Saudi Arabia who, secretly, and against advice, went to India to buy kidneys.¹⁵ Kidney trading in India¹⁶ and Hong Kong¹⁷ is confirmed by other investigators. The brisk business of buying human organs from the poor in Egypt was halted by a ban promulgated by the Egyptian Society of Nephrology.¹⁸

Cash rewards for organs have been proposed in the United States although Congress banned the buying and selling of human organs with the 1984 National Organ Transplant Act. Although payment for organ donation is judged anathema by many people, a death benefit payment of \$1,000 has been suggested to motivate families of potential organ donors.¹⁹ Laws now prohibiting organ brokerage and assuring fair organ allocation would continue unchanged. A death benefit payment, it is further proposed, may most favorably affect the socially disenfranchised through increased donation and transportation of organs in minority populations. The risk to society, it is argued, from such a death benefit payment is extremely small, and the potential benefit to patients whose lives would be saved is enormous.¹⁹

Such a proposal, however, is considered by some to be "logically, ethically, and practically flawed."²⁰ Payment is a type of coerced altruism, undermines the consent process, encourages a black market of covert payments for organs, and raises a series of "slippery slope" questions.²⁰

Other suggested forms of monetary donor compensation include assistance in the payment of funeral expenses, a cash award to the estate of the donor, a cash award to a charity of the donor or the family's choice, or a limited low-cost life insurance policy redeemable on the donation of organs by the deceased policy holder.²¹ Concern has been expressed about the impact of financial incentives on the cost of already expensive transplant procedures.²²

Proponents of donor compensation point to the longstanding practice of paying for blood products and human sperm. Proponents also argue that the moral objections are overestimated and that the concern for the reversal of altruism is unfounded. Furthermore, it is morally wrong to let thousands of patients die for lack of donor organs.²³ Certainly organs should not be placed on the block with bids and donation going to the highest bidder. The quality of the nation's blood supply improved dramatically with the virtual elimination of paid blood donors when the FDA required donor bags to be labeled, "volunteer" or "paid" in terms of source. Paid donors also have a high incidence of positive reactions for infectious disease markers, especially hepatitis B.²⁴ Opponents of donor compensation argue that it is morally reprehensible, damages American public altruism, would lead to unequal distribution of organs to the affluent part of society, and might lead to coercion, violation and exploitation.²⁵ Most of the arguments on both sides of this issue are based on personal beliefs and anecdotal evidence. Often the debate confuses the issue of supply (shortage) with the issue of demand (allocation).²¹

PRESUMED CONSENT

Another method to increase the supply of organs is to assume that all competent adults consent to donate their kidneys and perhaps other organs in the event of a fatal accident, unless they have refused in writing. No family consent is required. This is known as opting out, as opposed to the opting in approach where individuals are asked to decide whether or not they wish to donate their organs after death. Opting out legislation is in effect in Austria, Bel-

gium, Denmark, Finland, France, Norway, and Singapore. In Belgium, organ donation increased 119% in the first three years after implementation of the law.²⁵ In Singapore, the law resulted in a steadier supply of kidneys and also increased significantly the number of transplants.²⁶

Attempts to pass such legislation in the United States have so far failed,²¹ although proposals concerning presumed consent were already advanced in the medical literature a quarter of a century ago.²⁷ Such proposals were then met with strong opposition²⁸ but continue to be made. The advantages of presumed consent include reduction of the emotional burden on families and physicians, increased acceptability by the family of a "routine procedure," avoidance of delay in finding family to obtain consent, and preservation of the right to refuse for those who do not wish to donate.²⁹

Opponents to presumed consent argue that "there are good moral and practical reasons why presumed consent is an idea whose time has not come and why other approaches, including a truly systematic effort to ask about donation while patients are still alive and competent are better, morally more defensible, and more effective."³⁰ These investigators assert that consent cannot be presumed, and it is simply wrong to presume that a deceased person or his/her next of kin would consent to use of the organs. A recent survey of the general public showed that only 39% of respondents favored presumed consent.²¹ Thus, other alternatives need to be found. Proposed alternatives to presumed consent include maximizing actual consent, requiring that next of kin be asked to donate organs, and routinely requesting organ donations of competent persons.³⁰

ORGAN TRANSPLANTATION AND BLACKS

The difficulty in finding well-matched kidneys for transplantation into black Americans is compounded by the disproportionately low rate of black donation. Several studies have shown that blacks are neither transplanted nor represented on kidney transplant waiting lists in numbers that reflect their proportion of the population on dialysis.³¹ The principal reasons for the reluctance of blacks to give permission for organ donation are a lack of awareness of the status of organ transplantation and the urgent need for organs by blacks, religious beliefs and misperceptions, distrust of the medical establishment, fear of premature declaration of death if a donor card has been signed, and a preference among black donors for assurance that the organs will be given preferentially to black recipients.³² Additional reasons include an unwillingness to think about death, and the fear that a donor might not receive adequate medical care.³¹

Several affirmative action programs for kidney allocation have been suggested.³¹ A grass-roots approach with well-organized organ donor campaigns in the black population, a committed private sector and a volunteer community effort, has also been proposed.³² Certainly, every effort should be made "to ensure that the organ distribution system is just, that the rate of organ donation by minorities is optimal and that ongoing research provides us with additional knowledge that can be used to eliminate any racial disparities in organ transplantation."³³

WORLD HEALTH ORGANIZATION

On May 13, 1991, the World Health Assembly endorsed a series of guiding principles on organ transplantation

intended to provide an orderly, ethical, and acceptable framework for regulating the acquisition and distribution of human organs for transplantation.¹³

The World Health Organization allows organ harvesting for transplantation either after explicit consent (opting in) or with presumed consent (opting out) provided there is no opposition from the donor or the family. Physicians determining the death of the potential donor or caring for the potential recipient should not be directly involved in the transplantation procedure. Adult living donors may be used if informed consent is given freely by the donor without undue influence or pressure. Minors should not be used as organ donors except in the case of regenerative tissues. Giving or receiving payment for organs should be prohibited. Donated organs should be made available to patients on the basis of medical need and not on the basis of financial or other considerations, thus ensuring distributive justice and equity.

NEW YORK STATE INITIATIVES

On August 2, 1985, Governor Mario Cuomo signed the Request for Consent to an Anatomical Gift Act into law. The Act, generally known as the "Required Request Law," obligates hospital personnel to request consent for organ and tissue donation from the family members of a deceased patient if the deceased is a suitable candidate for donation. New York was the second state in the nation to pass the law and the practical and ethical questions associated with its implementation were unexplored. Governor Cuomo asked his Task Force on Life and the Law to propose policies for the law's implementation.

In response, the Task Force examined the process in the State to procure and distribute organs and the broad policy questions raised by the potential increased supply of donated organs and tissues. During that initial inquiry, the Task Force identified several issues of pressing concern. It then undertook a two-year study of organ and tissue transplantation in New York State.

The Report of the Task Force³⁴ describes the existing system in New York State to procure and distribute organs. It also sets forth the Task Force's recommendations to restructure that system with respect to three broad areas of concern: public health issues regarding the procurement process, the need to enhance coordination and centralization in the procurement system, and policies to ensure equitable access to the scarce supply of organs. In addition, the Report describes current programs for tissue procurement and addresses the need for sound public policies and oversight. The Task Force proposed that its recommendations should be achieved through an executive order, legislation, and regulation.

On the basis of the recommendations of the Task Force, the Organ and Tissue Procurement Bill was introduced in the New York State legislature in 1990. The Bill was adopted on July 4, 1991, as Article 43-13 of the New York Public Health law. The law (i) ensures equitable access to donated organs among patients waiting throughout the state for a donated organ, (ii) establishes public oversight and standards for the procurement and distribution of tissues for transplantation, and (iii) creates a special council to address the ethical and social issues at the frontier of evolving transplant technology.

Previously there was regional disparity with larger numbers of patients on waiting lists in New York City versus upstate New York. This fact was perceived as a potential

inequitable drain on available organs from upstate to New York City. Specific measures in the new law to ensure equity include a ban on multiple listings and the requirement that lists of patients awaiting transplantation be aggregated at the organ procurement organization level, rather than by each transplant center. Standards are also being developed to screen tissue donors.

FEDERAL INITIATIVES

A federal Task Force on Organ Transplantation was appointed in 1984 and issued a report in 1986.³⁵ The report resulted in the creation of the Organ Procurement and Transplantation Network (OPTN) in 1987. The OPTN has operated under contract with the Department of Health and Human Services (DHHS) by the United Network for Organ Sharing (UNOS), a private, non-profit organization. All US transplant centers and organ procurement organizations (OPOs) are required to be members of the OPTN, register each potential transplant recipient on the UNOS computer, and provide information on each organ donor and recipient to the UNOS database.¹²

A variety of federal legislative efforts to increase donor supply has been far from successful. These include the National Organ Transplant Act of 1984, the Organ Transplant Amendments Act of 1988, and the Transplant Amendments Act of 1990.¹¹ A report of the DHHS, released in March 1991, states that "current organ distribution practices fall short of congressional and professional expectations."³⁶ Although the supply of donor organs has increased a little in recent years, it remains much lower than the actual needs. Efforts at improving the donation rate are ongoing in many states and are most successful in Arizona, North Dakota, West Virginia, New Mexico, and Nevada.¹¹

In July 1991, the Office of the Surgeon General of the US Public Health Service, in collaboration with the Health Resources and Services Administration's Division of Organ Transplantation, hosted a two-day workshop to assess issues surrounding low donation rates, develop recommendations and strategies, and help increase donation rates.¹ The work group specifically recommended the following:

- The surgeon general should become the national spokesperson for organ donation.
- A national effort should be mounted to encourage the signing and carrying of organ donor cards.
- Minority living-related donors and recipients should participate in public education to overcome major obstacles such as fear of death among the affected populations.
- Culturally sensitive and ethnically similar transplant coordinators and health care professionals should be recruited.
- The term "brain death" should be eliminated.
- Bilingual consent forms and donor cards should be made available.
- Uniform standards for individuals making requests of potential donor families should be developed.
- A strategy for increasing hospital compliance with current statutory and regulatory requirements of "routine inquiry" and "required referral" should be developed.
- The three-year Medicare eligibility limit for transplant recipients should be eliminated, and coverage for immunosuppressive medications for patients should be made coterminous with the period of entitlement.
- A relationship between the local medical examiner or coroner's office and organ procurement community should be established.
- Health donors at both ends of the age spectrum should be used.
- Organs and tissues from hepatitis-C-positive donors and donors with systemic infections should be used selectively.
- The benefits of live donations and the superior long-term graft

survival rates relative to renal transplantation should be made available to the public.

- Financial disincentives to live organ donation should be eliminated.

The Surgeon General considers this "a comprehensive blueprint for implementing activities geared toward increasing donation."¹

In December 1991, a meeting was convened in Atlanta by the Centers for Disease Control at which public and private health officials discussed and made recommendations about a national tracking system for transplanted organs and tissues. A vital component of this proposed system is the introduction of consistent post-transplant HIV testing for recipients of donor organs and tissues.³⁷

MORAL ISSUES

A heated debate recently took place about whether or not alcoholics should compete equally for liver transplantation. Moss and Siegler proposed that patients who develop end-stage liver disease through no fault of their own should have higher priority for receiving a liver transplant than those whose end-stage liver disease results from failure to obtain treatment for alcoholism.³⁸ These investigators present arguments about fairness (eg, people must be held responsible for their behavior) and about the need for careful allocation of finite resources. They believe that only patients who are abstinent and who have not been offered previous treatment for alcoholism should receive grafts, and then only as part of prospective clinical studies.

Cohen and Benjamin reject these proposals and argue that the statements that alcoholics are morally blameworthy and will not have satisfactory survival rates after liver transplantation are defective.³⁹ These investigators assert that there is no good moral or medical reason for categorically precluding alcoholics as candidates for liver transplantation. One should no more deny such a therapeutic option to an alcoholic than one would deny treatment to a car accident victim who was not wearing a seat belt. Can one morally withhold treatment from a lung cancer patient who is a heavy smoker? Equitable allocation of organs based on moral virtue is impossible because there are no guidelines or standards to measure such virtue.⁴⁰

Caplan points out that a number of moral and public policy assumptions about the demand for and the supply of organs are false or questionable.⁶ These include the assumptions that Americans know a great deal about transplantation and the need for organ donations, that obtaining a license for driving a motor vehicle and organ donation mix, and that there is lack of coordination among the agencies involved in procurement. Voluntary choice and altruism are still the American foundations for organ donation in spite of proposals to use financial incentives to encourage organ donation or to adopt the policy of presumed consent.

Obtaining organs is clearly not the only goal of public policy with respect to cadavers, continues Caplan. If that were the sole goal, public policy would allow physicians to simply take what they want from cadavers without permitting any objections or exceptions. Individual choice is still "the preeminent value reflected in our public policy and morality with respect to procurement."¹⁰

The Committee on Bioethical Issues opposes the notion of presumed consent on moral grounds. The most important tenet of our ethical system in the West is the primacy of rights over utility (ie, individuals have rights that may not be sacrificed even in the furtherance of the common good). Control over and propriety over one's own body parts must

be regarded as a most fundamental right. Even in death, individuals do not give up their rights: decision-making over one's body does not revert to the state but reverts to the person the deceased may have designated in advance or to the next of kin.

Another reason to oppose the notion of presumed consent is the "slippery-slope" argument. Loss of recognition of the absolute right of an individual to his own body at the moment of death to further the interest of the community may result in erosion of our respect for rights in other instances. Would healthy individuals be compelled to give blood transfusions when there is a shortage of blood? Would an individual with two good kidneys be forced to give up one? Furthermore, if the rights of the dead are sacrificed, concern can be raised that rights of others who are weak, such as the retarded, and the elderly patient with Alzheimer's disease, might be easily sacrificed in the pursuit of usable body parts. This concern is even greater with the emergence of new technologies in that the notion of "presumed consent" could be expanded so that the rights of these individuals are sacrificed.

We have previously written about some of the ethical dilemmas concerning the scarcity of medical resources.⁴⁰ The scarcity of organs is an important example of this problem. Unlike many other scarce medical resources such as ICU beds or dialysis machines, the problem of scarcity of organs cannot be easily corrected by a commitment of financial resources. We can build more ICU beds and purchase more dialysis machines as needed. However, the supply of organs will remain less than the demand no matter how successful efforts are in recruiting new organ donors. How then should these organs be distributed?

Individuals have a right to designate the recipients of their organs. A father may designate his daughter as the recipient of the donation of one of his kidneys in preference to all others. Controversy arises in cases where a specific recipient of a donated organ is not designated by the donor: for example, if the donor has signed a donor card in the event of his death. Innumerable formulas for the "just" distribution of scarce resources have been devised, based on various conceptions of "equality," "utility," "need," and so on.⁴¹⁻⁴³ We agree with those ethicists who argue that the notion of "distributive justice" is itself "immoral." Nozick, for example, shows that the implementation of any formula of "distributive justice" leads to unjust results.⁴⁴

We believe that medical criteria are the single most important criteria to decide who gets an organ when a specific recipient has not been designated by its donor. If there are two candidates for an organ who have equivalent medical conditions, the recipient should be decided on a "first-come, first-serve" basis.

CONCLUSION

It is highly unlikely that the donation environment would be favorable to public policy proposals that call for drastic shifts away from the prevailing ethics of voluntary choice and altruism.¹⁰ The general level of public support for organ donation is not reflected in the low frequency of donation and the choices that families make when a death occurs. Presumed consent and/or financial compensation to encourage organ donation do not seem to be supportable alternatives by the United States public and professional communities.

The Surgeon General of the United States stated that success in increasing organ donation requires the continual dedication, expertise, and commitment of both the federal

government and the private sector.¹ A sensitive, multidisciplinary, family-centered approach when raising issues about organ donation with grieving relatives is presently being explored. Such a pilot scheme in Kentucky resulted in a nearly 30% increase in organ donation over 18 months, whereas the national donation rate declined during that period.⁴⁵

Physicians' attitudes and approaches are also pivotal in procuring organs for transplantation. Families are more receptive to donation if there is warm rapport between them and the medical staff throughout the patient's hospitalization. Hence, it has been suggested that efforts be focused on smaller hospitals where, although death may not be as common, the setting is likely to be more supportive of the family involved.⁴⁶ The required request law in New York was amended in 1991 to recognize the critical role that the family-physician relationship can play. The law was amended to allow physicians to request organ donation even if the physician determines and certifies the death of the patient, provided that the physician is not involved in the organ transplant in any way.

Medical and nursing schools should include all aspects of organ and tissue donation in their curricula, stressing the importance of effective, sensitive, and timely communication about donation. UNOS is currently developing such a curriculum for medical and nursing students.⁴⁶

The soft approach of asking family consent for organ donation is still ethically superior to presuming consent.²⁶ Maximizing actual consent, requiring requests of next of kin and routine requests of competent persons are normally acceptable methods of attempting to increase organ donation.³⁰ Education and appeals to altruism are the main ethical methods to increase the supply of organs since "a policy that resorts to monetary inducements, that replaces altruism by selfish self-interest and that manipulates consent by monetary incentives, has too many ethical liabilities to be acceptable either as a policy or an experiment."²⁰ Today's greatest challenge in organ transplantation is not in the medical arena. Instead, the single most important method of increasing organ donation is in the education of physicians about the need for organ transplants.⁴⁷ Physicians should feel that it is their ethical duty to seek consent for donation. Increasing organ donation is an important issue for medical educators.⁴⁸

REFERENCES

- Novello AC: Increasing organ donation: a report from the Surgeon General's workshop. *JAMA* 1992; 267:213.
- Cooper DKC: Experimental development of cardiac transplantation. *Brit Med J* 1968; 4:174-181.
- Shimon DV, Admon D, Zilberman S, et al: Heart transplantation: state of the art. *Israel J Med Sci* 1989; 25:575-582.
- Burdine J, Fischel RJ, Bohman RM III: Cardiac transplantation. *Crit Care Clin* 1990; 6:927-945.
- Hunt S, Billingham M: Long term results of cardiac transplantation. *Ann Rev Med* 1991; 42:437-447.
- Fragomeni LS, Bonser RS, Kaye MP: Clinical results of heart-lung transplantation. *Progr Cardiovas Dis* 1990; 33:97-103.
- Reichenspurner H, Meiser B: Heart-lung transplantation in 1990—Indications, surgical techniques, postoperative complications and outcome. *Thorac Cardiovasc Surg* 1990; 38:271-275.
- Cosimi AB: Update on liver transplantation. *Transplant Proc* 1991; 23:2083-2090.
- Najarian JS, Matas AJ: The present and future of kidney transplantation. *Transplant Proc* 1991; 23:2075-2082.
- Caplan AL: Assume nothing: the current state of cadaver organ and tissue donation in the United States. *J Transplant Coop* 1991; 1:78-83.
- Evans RW, Orians CE, Ascher NL: The potential supply of organ donors. An assessment of the efficiency of organ procurement efforts in the United States. *JAMA* 1992; 267:239-246.
- Sanfilippo FP, Vaughn WK, Peters TG, et al: Factors affecting the waiting time of cadaveric kidney transplant candidates in the United States. *JAMA* 1992; 267:247-252.
- Anonymous: World Health Organization guiding principles on human organ transplantation. *Lancet* 1991; 337:1470-1471.
- Salahudeen AK, Woods HF, Pingle A, et al: High mortality among recipients of bought living unrelated donor kidneys. *Lancet* 1990; 336:725-728.
- Mohamed AS, Velasco N: Kidneys for sale. *Lancet* 1990; 336:1384.
- Kandela P: India: kidney bazaar. *Lancet* 1991; 337:1534.
- Lam SK: Kidney trading in Hong Kong. *Lancet* 1991; 338:453.
- Anonymous: Egypt acts to curb buying of organs from the poor. *American Medical News* February 10, 1992, p27.
- Peters TG: Life or death: the issue of payment in cadaveric organ donation. *JAMA* 1991; 265:1302-1305.
- Pellegrino ED: Families' self-interest and the cadaver's organs: what price consent? *JAMA* 1991; 265:1305-1306.
- Kittur DS, Hogan MM, Thukral VK, et al: Incentives for organ donation? *Lancet* 1991; 338:1441-1443.
- Evans RW: Incentives for organ donation. *Lancet* 1992; 339:185.
- Caplan AL: Sounding board: ethical and policy issues in the procurement of cadaver organs for transplantation. *Hum Organ Transpl* 1987; 272:275.
- Blood Policy and Technology Washington DC: US Congress, Office of Technology Assessment, OTA-H260, January 1985.
- Roels L, Vanrenterghem Y, Waer M, et al: Three years experience with a "presumed consent" legislation in Belgium: its impact on multiorgan donation in comparison with other European countries. *Transplant Proc* 1990; 22:2078-2079.
- Teo B: Organs for transplantation. The Singapore experience. *Hastings Center Rep* 1991; 21:10-13.
- Dukeminier J Jr, Sanders D: Organ transplantation: a proposal for routine salvaging of cadaver organs. *N Engl J Med* 1968; 279:413-419.
- Sadler AMJ, Sadler BL, Stason EB, et al: Transplantation: a case for consent. *N Engl J Med* 1969; 280:862-867.
- Spital A: The shortage of organs for transplantation: where do we go from here? *N Engl J Med* 1991; 325:1243-1246.
- Veatch RM: Routine inquiry about organ donation an alternative to presumed consent. *N Engl J Med* 1991; 325:1246-1249.
- Arnason WB: Directed donation: the relevance of race. *Hastings Center Rep* 1991; 21:13-19.
- Callender CO, Hall LE, Yeager CL, et al: Organ donation and blacks: a critical frontier. *N Engl J Med* 1991; 325:442-444.
- Kasike BL, Neylan JF III, Riggio RR, et al: Effect of race on access and outcome in renal transplantation. *N Engl J Med* 1991; 325:429.
- The New York State Task Force on Life and the Law: Transplantation in New York State: *The Procurement and Distribution of Organs and Tissues*. New York, NY, Jan 1988, p 168.
- Task Force on Organ Transplantation: *Organ Transplantation: Issues and Recommendations*, Rockville, MD, Health Resources and Services Administration, 1986.
- Office of the Inspector General-The Distribution of Organs for Transplantation: Expectations and Practices. Washington, DC: Office of Analysis and Inspections; 1991. US Dept of Health and Human Services, publication OE1-01-89-00550.
- Voelker R: Organ, tissue tracking system on way. *American Medical News* Jan 13, 1992, pp 7,9.
- Moss AH, Siegler M: Should alcoholics compete equally for liver transplantation? *JAMA* 1991; 265:1295-1298.
- Cohen C, Benjamin M: Alcoholics and liver transplantation. *JAMA* 1991; 265:1299-1301.
- Rosner F, Sordillo PP, Sechzer POH, et al: The allocation of scarce medical resources. *NY State J Med* 1990; 90:552-558.
- Vlastos G: Justice and equality, in Brandt RB (ed): *Social Justice*, Englewood Cliffs, NJ, Prentice Hall, 1962, pp 31-72.
- Rescher N: *Distributive Justice*, Indianapolis, Bobbs Merrill, 1966.
- Basson MD: Choosing among candidates for scarce medical resources. *J Med Philos* 1979; 4:313-333.
- Nozick R: *Distributive Justice. Anarchy, State, and Utopia*, New York, Basic Books, Inc, 1974, pp 149-231.
- Anonymous: Ethical conundrums in liver transplantation. *Lancet* 1991; 337:1030-1031.
- Randall T, Marwick C: Physician's attitudes and approaches are pivotal in procuring organs for transplantation. *JAMA* 1991; 265:1227-1228.
- Randall T: Too few organs for transplantation, too many in need. . . and the gap widens. *JAMA* 1991; 265:1223,1227.
- Novello AC, Braslow JB: Increasing organ donations. An important issue for medical educators. *Acad Med* 1992; 67:314-315.

The story of Lassa fever

Part IV: The politics of research

JOHN D. FRAME, MD

What was known of Lassa fever (LF) by 1974 had for the most part been learned from hospital outbreaks in Nigeria, Liberia, and Sierra Leone. Serological studies had also been conducted as a means of elucidating the distribution and prevalence of LF in Africa. They demonstrated that LF had been common in parts of Nigeria well before the 1969 and 1970 outbreaks in Jos and that cases had occurred among missionaries in Guinea (Fig 1).¹ Our survey of mission hospitals and missionaries on furlough added six countries to the four already known Lassa virus (LV) endemic areas.²

As yet, however, except for the epidemiological studies conducted in Liberia and Sierra Leone at the time of the outbreaks there, no direct field studies of LF had been launched in Africa. Fascination with the new disease had not yet brought funding. To be sure, there was considerable interest in the significance of LF in some quarters.

The US Central Intelligence Agency (CIA) was very interested, apparently as a part of its general intelligence gathering mission. A CIA representative visited me twice, first to discuss what the outbreaks in Nigeria might mean in terms of infectious disease in West Africa, and later, whether my finding evidence of LV infections in missionaries in Ivory Coast, Mali, and Burkino Faso indicated the spread of the disease up the Niger River. I explained that LF was probably not a new disease, spreading across West Africa, but an old disease whose distribution was just now being clarified.

As a result of the publicity surrounding the entry of LF patients to the United States and Great Britain, the African countries which stood to gain most from LF research seemed loath to acknowledge that the disease might pose a serious public health problem to them. They were concerned that acknowledgment of the presence of LF would damage their efforts at developing tourism and commerce, and also reflect poorly on their level of development.

Once the magnitude of the public health problems LF posed in West Africa began to be seen, development of a vaccine for its control seemed appropriate. It was not clear at the time whether a vaccine could indeed control all LV infections; the presence of various LV serotypes was suspected but not yet certain. A more immediate concern was the risk incurred by laboratory investigators. Fraser, Campbell, Monath et al reflected this concern in stating

that because of the hazard of working with LV a safe and effective vaccine would not be available in the near future.³

I was trying to find a "handle" on the problem that would a framework for investigation and attract funding. The project involving the serological survey of missionaries and mission hospitals was taking all the time I could spare from my livelihood, my medical practice. However, it was clear that within a year or two the survey would bring decreasing results. I began to think of the next possible step. I was not a virologist with access to a high-containment facility, nor the competence to use it. The idea, how I could continue in LF research, came to me in an unexpected way.

DREAMING UP A RESEARCH PROPOSAL

One day in July 1973, I awoke at about two in the morning with a complete research proposal in my mind, rose, and typed it out in the next two hours, then returned to bed. The program I prepared was one of identifying convalescents from LF and producing LF immunoglobulin (LFIG) from plasma obtained by plasmapheresis. I believed that funding might become available since such a program would supply virologists with material for investigations of LV in tissue culture and animal models, and plasma for their protection in case of accidents.

The proposal incorporated elements of case-finding and epidemiology to identify the fairly large number of donors who would be needed. I knew that plasmapheresis might be opposed on cultural grounds. However, it was already clear from our experience in Nigeria that Africans could be induced to donate plasma.

The next morning I was convinced that a proposal so "dreamed up" would have little value; I did not even review it. A month or so later I took the proposal out of my drawer. I was delighted to find that it did indeed have merit. However, I had no time then to tackle another project.

Occasionally I refined my draft proposal, and a year later, in June 1974, I mentioned it to Dr Michael Katz, Chairman of the Division of Tropical Medicine at Columbia University. I suggested that the proposal should be examined by the scientists at the Yale Arbovirus Research Unit (YARU), who had been deeply involved with our research. So it was that we asked Dr Robert E. Shope, now the director of YARU, and Dr Wilbur Downs and Dr Jordi Casals to join Katz and me for a review of my suggested research program.

After intensive review the group generally approved of the proposal. Shope said that analogous investigations of Bolivian hemorrhagic fever (BHF) by Dr Gerald Eddy of the US Army Medical Research Institute of Infectious Diseases (USAMRI-ID) had been successful. However, the group suggested that the program be divided; an initial small pilot project should test the feasibility of finding donors and obtaining plasma. It would be easier to gain funding for such a small program than

From the Division of Tropical Medicine, Columbus University School of Public Health, New York, NY 10032.

Address correspondence to Dr Frame, 152 Slocum Crescent, Forest Hills, NY 11375.

Part III appeared in the October 1992 issue.

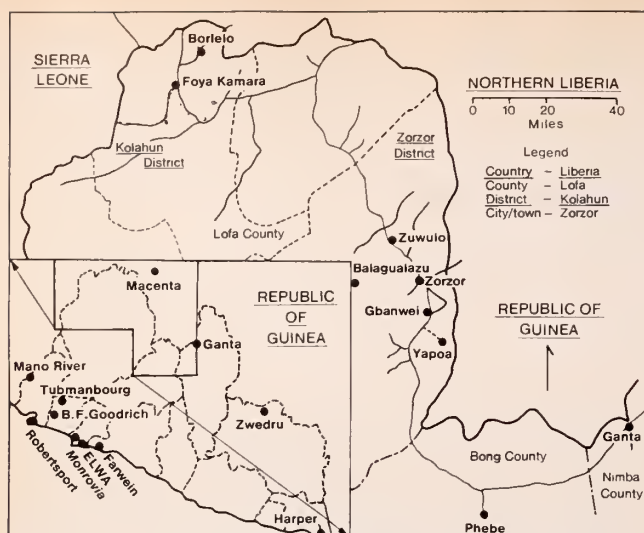


FIGURE 1. Map of Liberia (courtesy, Transactions of the Royal Society of Tropical Medicine and Hygiene).

for the whole. Once the feasibility had been established, funding for the major program would more likely be available. There was one significant limit to what I suggested. The investigation required culturing LV in a laboratory with containment facilities for viral research. I knew that all research with live LV at Yale had been suspended in 1969 after the death of the technician Juan Roman. To carry the plan forward I required the assistance of the US Centers for Disease Control (CDC). I was startled at Downs' reaction, that if I proposed a joint program with the CDC, I would probably be excluded. I asked what other laboratory might be available. However, he had no suggestions in that regard.

Shope subsequently wrote, confirming his general approval of the project, and noting that I should have a firm commitment from the CDC for a supply of inactivated antigen for testing, and a willingness to perform neutralization tests. I also needed to enter into an agreement with the government of the country that was to be the site of my program.⁴

After making the suggested revisions, I called Dr Herta Wulff, the virologist in charge of the maximum security laboratory at the CDC, in December, asking whether I might send her my proposal. However, she was about to leave on vacation. Furthermore, the laboratory in Atlanta was being refurbished, and she was working on problems related to the development of a new testing system for the diagnosis of LF. She suggested I forward my proposal in early 1975 after her return. I did this but received no response. I therefore called her in late January.⁵

Wulff told me that the CDC could not enter into a project with me since reconstruction of the containment laboratory would probably not be completed until the autumn. I responded that I would not be ready to start the proposal until the autumn at the earliest as I was still looking for funding. She then informed me directly that the CDC could not work on a joint program with me.⁶

At about that time Dr David Van Reken, my niece's husband, was a fellow in infectious diseases at the Naval Hospital Norfolk, Virginia. He accompanied his chief on a trip to the facilities of USAMRIID at Fort Detrick, Frederick, Maryland. He mentioned to Dr William Beisel, Scientific Advisor to the Commanding Officer, that his uncle was the person who had developed the program in which LF was found, and asked whether USAMRIID was at all interested in working with this virus in their containment facility. Beisel said that USAMRIID would be interested in hearing from me.

In the meanwhile, I was seeking funding. A foundation which had an interest in missionary health and which had funded a small program of mine earlier was no longer supporting health care activities. I sent a copy of my proposal to Eddy at USAMRIID; he responded that he and his colleagues were discussing entering into a program of LV vaccine development. If a decision were reached, USAMRIID would be interested in collaborating with me. In a postscript, he noted that Dr Karl Johnson, who had previously worked with BHF, would be starting as head of a LF program at the CDC in September 1975.⁷

THE ARENOVIRUS SYMPOSIUM IN ATLANTA

In the late winter, I was invited to contribute to a Symposium on the Arenoviruses of Public Health Importance to be held in Atlanta, July 14-16, 1975, under the joint sponsorship of the CDC and the World Health Organization (WHO). With the discovery of the hemorrhagic fever viruses of this group in Argentina, Bolivia, and Africa, as well as of other agents of lower human pathogenicity, a symposium might help in research among all of them. Among those in attendance were researchers and public health officials from Argentina and Bolivia, as well as from Nigeria, Sierra Leone, and Liberia. It was hoped that the open discussions would overcome the hesitation of the African governments toward allowing research on LF in their countries.

An important advance reported by Dr Herta Wulff at the symposium was the development of an indirect fluorescent antibody (IFA) test for LF.⁸ In the following discussion, a question was raised whether the antibody was induced by an antigen other than that measured by complement fixation (CF).

This was not yet clear. Dr Thomas Monath of the CDC noted that while Wulff's IFA test showed no difference between LV types from Sierra Leone and Nigeria, differences had been found by CF. It was also reported that the test could not yet be certified for use in most laboratories. In some cases, culture of material scraped from the reagent slides had shown persistent viral activity, and a method of inactivation without loss of diagnostic sensitivity was still being sought.

My contribution to the symposium was a report of the surveillance for LF among missionaries in West Africa.⁹ The meeting had a significance for me that I began to realize before it was over. It was here that I first met Dr Paul Mertens of the Curran Lutheran Hospital (CLH) in Zorzor, Liberia where the 1970 outbreak had occurred. On questioning, he told me of plasmapheresis he had carried out at CLH; Liberians could be persuaded to donate plasma.

I also met Karl Johnson whose work with the Machupo virus of BHF I knew from the meetings of the American Society of Tropical Medicine and Hygiene. In fact, he had acquired the disease himself. It was he who had suggested that convalescent plasma be given to Jordi Casals early in his bout with LF in 1969. I had heard that the Middle America Research Unit where he had worked had been disbanded. Johnson told me that in February he had approached the CDC and had been informed there was no place for him there. However, in March he was asked to join a program of LV research at the CDC.

The first aspect of the CDC program would likely be the collection of convalescent plasma. The agency was considering where to conduct the project. Its investigation of LF in

Sierra Leone in 1972³ indicated prospects of finding enough LF cases there to ensure a good supply of convalescent plasma. There was, however, some uncertainty whether Sierra Leone would agree to LF research within its borders.

Among those whom I met at the symposium was Mr J. Robert Ellis, Director of Preventive Services in the Ministry of Health and Social Welfare (MHSW) of the Republic of Liberia. He had been startled to learn from my paper of a LF case in Liberia. The patient was an African-American missionary in the Hayes Gowien Town Mission, a few miles from Monrovia, Liberia's capital. Many prominent and politically important Liberians owned farms in the area. In our conversations, he stated that he would discuss with the MHSW the possibility of LF research in Liberia.

Johnson had learned from Shope that I was hoping to begin research in LF myself. I told him I would likely try to start a program in Liberia if the CDC did not select that country as its research base, and he said he would let me know the country where his work would begin.

THE LIBERIAN INSTITUTE FOR BIOMEDICAL RESEARCH

In November 1975, Johnson informed me the government of Sierra Leone had agreed that the CDC might begin LF research there. I then wrote Ellis reminding him of our conversation in July, and asking whether the Republic of Liberia would accept a LF project.¹⁰ Ellis indicated the interest of the MHSW in my proposal; he asked that I correspond with Dr Emmet A. Dennis at the Liberian Institute for Biomedical Research (LIBR) (Fig 2).

A Liberian who obtained his doctorate in Parasitology at the University of Connecticut, Dennis was Associate Professor of Parasitology at Rutgers University. He was spending his sabbatical year organizing the LIBR (Fig 3). There had earlier been a Liberian Institute of the American Founda-

tion for Tropical Medicine funded by Harvey Firestone, located near the Firestone rubber plantation and Robertsfield International Airport. It had now been reborn as the LIBR, with the buildings and equipment of the old Institute. Dennis was seeking contracts with institutions outside Liberia to conduct research there, both to obtain external funding for the work of the LIBR and to assist in the training of research staff. Among them was the New York Blood Center (NYBC) which was entering on a research program for the development of a vaccine against hepatitis B virus infections.¹¹

Dennis believed a program to conduct LF research in Liberia would benefit the LIBR. He noted, however, that the primary interest in research in Liberia could not be the export of plasma and that as much of the investigation as possible should be carried out in Liberia. In the following months, we developed a research agreement between Columbia University and the LIBR. Most of the negotiations were by correspondence, although twice we met at Columbia when Dennis returned to the United States to further his own research plans and move his family to Monrovia. More revisions were made during my first trip to Liberia.

Now that an African country had been found where a program for plasmapheresis and the preparation of LFIG might be carried out, the need for funding became vital. Dr Lee Howard of the United States Agency for International Development (USAID) wrote that the agency might be willing to contribute to a program designed to assist the development of the LIBR, but that a request for help would need to come from the Republic of Liberia.¹² I forwarded the information to Ellis, although I recognized that even if USAID reached a favorable decision, a long and uncertain period of time would likely elapse before funds would be available.

HELP FROM THE ROCKEFELLER FOUNDATION

Then, Katz, my Department Chairman, arranged with Dr John Maier of the Rockefeller Foundation (RF) for an opportunity to present our proposal. Our plan was to

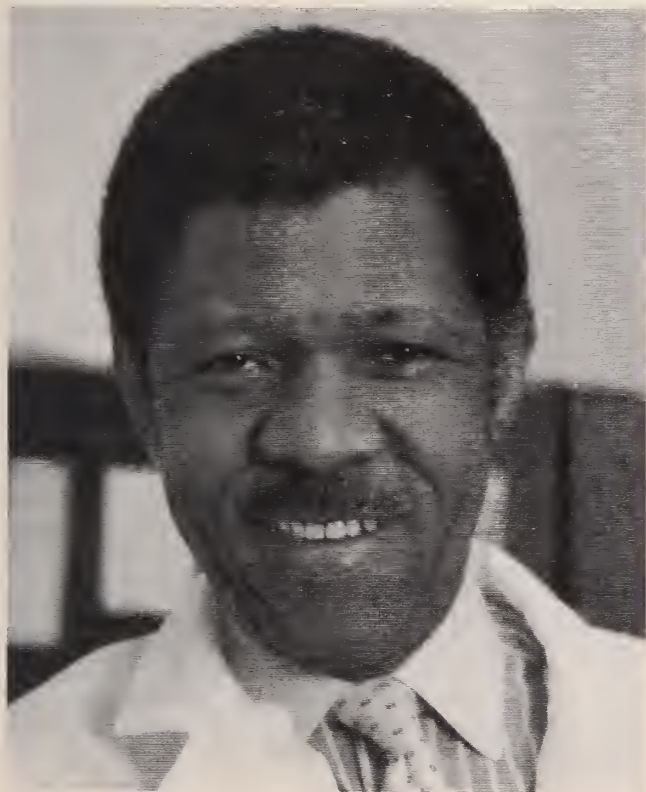


FIGURE 2. Emmet A. Dennis, Director, Liberian Institute for Biomedical Research (Emmet A. Dennis).



FIGURE 3. Bishop Bennie Warner, Vice-President, Republic of Liberia, at dedication of the Liberian Institute for Biomedical Research, December 12, 1978 (Emmet A. Dennis).

investigate the incidence of LF in Liberia, collect plasma from convalescents there, and fractionate the plasma to prepare immunoglobulin. A part of the immunoglobulin would be returned to Liberia for the treatment of patients there, and a part made available to researchers. Casals at YARU would identify LF patients by CF, and by Wulff's new IFA technique, if its safe use was confirmed by the CDC.¹³ Johnson, at the CDC offered to help with the IFA test until its safety could be confirmed and would supply Dr Casals with the reagent slides, once safety tests had been completed.

The RF agreed to grant \$35,000 for a one-year pilot study. The Foundation acceded to my request to delay the start of the program until September 1976, to permit completion of negotiations with the LIBR. Eventually, for reasons that will become clear, extensions without increase in funds were granted to permit work to the autumn of 1979.

A PROPOSAL FROM THE NYBC

In the summer of 1976, Dennis referred our proposal to Ms Betsy Brotman, Director of Virus Laboratory II (VILAB II), the local research unit of the NYBC. She responded with a review of some of the problems that would be confronted in research in Liberia. She then submitted a proposal for preliminary LF research in Liberia to be conducted under the aegis of VILAB II. She believed it would be difficult to persuade Liberians to submit to serological testing. She proposed conducting serological surveys of the staff and families of the Firestone Plantation, a few miles from the LIBR. Testing of employees from each of four neighboring counties would assure an unbiased sample from which the prevalence of LF in Liberia could be determined. Use of the facilities of the Firestone Hospital would simplify the process of obtaining specimens and transporting them to the LIBR for transshipment to the United States.¹⁴

I could not respond to the VILAB II proposal in detail before my impending departure to Liberia. I was already aware of most of the difficulties Brotman outlined. I had discussed them with Paul Mertens, with Katz, who had had research experience in East Africa, and with those who had been engaged in the BHF plasmapheresis program in Bolivia.

THE FIRST TRIP TO LIBERIA

In October 1976, I traveled to Africa for the first time; I had dreamed of such an occasion since I was a boy! Dennis and my niece, Ruth Van Reken, now living in Liberia, met me at Robertsville; the latter drove me to her home on the grounds of ELWA, the radio station of the Sudan Interior Mission located 10 miles out of Monrovia. This was to be my base of operations for the next three years. Dennis told me that he had presented our draft agreement to the MHSW. Dr M. Swamy, the Indian national employed as Epidemiologist by the Ministry, had in turn discussed the proposal with the WHO bacteriologist and epidemiologist in Monrovia; they had advised that it be rejected. They reasoned the proposal was too small and did not include enough epidemiology to benefit Liberia.

Under Dennis' guidance I met with the Minister, who was most cordial. The WHO Mission Chief in Liberia, Dr Karamoustakis, was also friendly; he had been out of the country when Swamy had approached the WHO Mission, and his group might have reacted differently if he had been

present. Perhaps, we could modify the proposal to satisfy his subordinates. Ellis authorized us to investigate the prevalence of LV infections in mission hospitals and those of the mining and rubber concessions, reporting all findings to the LIBR. He furnished us with a vehicle to visit the Hayes Gowien Town Mission near Monrovia where we had discovered an American serologically positive for LV.

Dennis and I revised our agreement to emphasize sero-diagnostic and incidence studies in hospitals. He also drove me to Phebe Hospital (PH), 115 miles up country, where I first met Dr Walter Gwenigale, the hospital director. I left a supply of vacuum tubes, needles, transfer pipets, and specimen vials sufficient to permit testing of the PH staff of about 250 workers and students. I also obtained sera from the staff of the hospital at ELWA.

During the visit I spoke on LF to the staff of the J. F. Kennedy Memorial Hospital in Liberia, and to the students of the small medical school. My niece's husband, David, suggested I substitute for him on a daily five-minute program, "A Visit with the Doctor," aired over ELWA, and enough discussions of LF were taped to permit a week of broadcasts. I continued these interviews in subsequent visits as a means of raising awareness of LF in Liberia.

When Dennis saw me off at the airport on my return to the United States, he was convinced that the MHSW would accept our revised proposal once it realized that a successful pilot study would likely lead to a far greater program.

In the following months, five of 92 Liberian staff members at the ELWA hospital were found to have LV antibodies (LVA). However, the news from the political front was discouraging. The MHSW was apparently increasingly disturbed at the small size of the proposed program in contrast to what the CDC was inaugurating in neighboring Sierra Leone and asked that agency to extend its work into Liberia; it was refused. The Ministry then re-typed our proposal as its own and submitted it to USAID, to have it rejected there on the grounds that there was no evidence LF was a public health problem in Liberia. Acting on the suggestion of Swamy, by then in charge of Preventive Services, the Foreign Ministry in March 1977 presented the proposal to a "major East European power" requesting its assistance in the investigation of LF in Liberia. This country agreed to send a delegation to work with the Liberians on this issue; the consultation was eventually scheduled for August or September 1977.

On its arrival in Liberia, the Soviet delegation was presented with the Liberian proposal. The delegation wanted the Liberians to commit themselves to Soviet help. The Liberians requested a program document which they could review. Then, in the autumn of 1977, I received a telephone call from Johnson at the CDC asking what was going on. Soviet colleagues had requested the CDC to supply 500 slides of LV antigen for IFA testing. In response to the CDC query regarding what research the group was contemplating, the Soviets responded that they expected to study the epidemiology of LF in Liberia. At about the same time, Johnson received a call from the CIA asking what the Soviets were doing with LF research in Liberia.

A SECOND TRIP TO LIBERIA, APRIL 1977

In the meantime, correspondence with Col Joseph F. Metzger, Commanding Officer of USAMRIID and with Gerald Eddy continued. Their initial willingness to purchase a small supply of LF immune plasma, made in the spring of 1976, was developing into suggestions for a major

program of two or three years' duration, if the initial studies in Liberia demonstrated an adequate number of potential plasma donors.

I went to Liberia in April 1977, uncertain as to what I could accomplish. I hoped that the prospect of a much larger program in Liberia on completion of the pilot study would encourage the MHSW to accept the research agreement between the LIBR and Columbia. Swamy was annoyed at my persistence and pointed out that since the Ministry of Foreign Affairs had already made overtures to the Soviet government, it would be impossible to grant Columbia the privilege of LF research.

On this trip, I learned that the preparation of LFIG had become a major issue in the consideration of the research proposal. In 1975, the World Health Assembly had warned developing countries against the practice of North American and European drug firms of obtaining immunoglobulin from poor residents of the Third World.¹⁵ The words, "immunoglobulin," in our proposal were now unacceptable. Dennis and I eliminated any mention of fractionation of plasma to produce LFIG in our new version of the draft agreement.

Dave Van Reken suggested that I travel up-country with Dr Ward Hurlburt who was working with USAID to help Liberia establish health centers in Lofa County where a major agricultural development project was in progress. On the way, we stopped at PH and learned that sera of about 240 staff and patients had been obtained and were awaiting testing. We then traveled to Zorzor. Dr Andrew Cole, a Liberian educated in the United States, was now the hospital director. I had corresponded with him earlier, and he now agreed to a serological survey of volunteers from the CLH staff. The next day, we traveled to the Swedish Free Pentecostal Mission Clinic in Foya Kamara, near the Sierra Leone border (Fig 4). Although the clinic did have a large outpatient program, its emphasis was on midwifery and child care. There I told what was known of LF, and I reminded them it had caused Esther Bacon's death. When I mentioned that hearing loss was a common complication of LF, they told me two of their midwives could no longer use their training because severe deafness had made it impossible for them to hear fetal heart sounds. All the staff who

were present on duty were willing to supply blood specimens (Fig 5).

On returning to ELWA, I rented a vehicle and driver from the YES Taxi Company and went back to Zorzor; 95 staff members wanted to be tested for evidence of infection with the virus that had killed their revered Miss Bacon. I then traveled to Ganta, northeast of Phebe, and visited the Methodist Hospital there. Even with short notice, most of the staff on duty agreed to submit to venipuncture. In all our staff surveys, the response was higher than expected by the hospital directors.

Although I was returning to the United States with 390 sera to be tested, I was not certain that the program would ever be acceptable to the Liberians. After Dr Casals had completed his tests, we knew that at least 63 of over 500 hospital staff tested so far had had LV infections, presumably enough to permit the start of a plasmapheresis program.

At this time of uncertainty, I wrote Dennis suggesting that a way out of the impasse regarding LF research in Liberia might be a direct request from President William R. Tolbert of Liberia to President Jimmy Carter asking for assistance in the production of a vaccine against LF, by now clearly a Liberian public health problem. I advised that President Carter first be told of USAMRIID's interest in preparing a vaccine.¹⁶

KEEPING A LOW PROFILE

Discussions with USAMRIID were proceeding steadily, although slowly. However, it was not at all clear that LF research in Liberia would become possible. When I returned to Liberia in October 1977, Dennis advised that I keep a low profile. He arranged, however, that I fly to Yekepa in Nimba County, and Buchanan on the coast, to conduct serological surveys of the staffs of the hospitals of the Liberian American Mining Company. I was received cordially by Dr Varsay Sirleaf and Dr Jan Ekengram, directors of these institutions. A friend of Emmet Dennis, Dr J. M. Bankole Jarrett of the hospital of the Bong Mining Company, had heard of my work and asked that his staff be tested. Dr Charles Harding of the Maternity Center in Monrovia also asked for a survey of his staff. I was



FIGURE 4. Testing for LVA at the Swedish Free Pentecostal Mission Clinic, Foya Kamara, Liberia. Dr Frame and missionary midwife Selma Erikssen (John D. Frame).



FIGURE 5. Christine Henne, a midwife at the Swedish Free Pentecostal Mission Clinic who has never heard her child cry out; she suffered total hearing loss from Lassa fever (John Frame).

uncertain whether to do this, in view of the limitations on my research prescribed by Ellis but finally acceded to Harding's request. The 330 specimens obtained on this trip yielded another 18 sera positive for LVA.

Dennis had planned the excursions so that I might meet Sirleaf and Jarrett, both on the LIBR Board of Directors, to explain the program and its significance for Liberia. In December 1977, the Board authorized Dennis to proceed with the project as a part of the LIBR program.

The Soviet team returned to Liberia in early 1978, announcing they were ready for research, and presented the Liberians with a list of personnel, vehicles, and laboratory and office equipment they expected to be supplied them. The Liberians reexamined the draft agreement with Columbia, and realized that in our proposal we would supply all these. Swamy tried to delegate the embarrassing task of rejecting the Soviet plan to Dennis, who refused to bear the onus. He suggested that Swamy could tell the visitors that Liberia had asked for a proposal to be studied and was not yet ready for a research team.

When I returned to Liberia in March 1978, Dennis again escorted me and our draft proposal, revised again, to the Division of Preventive Services, where it was initialed by the two of us and a glum Swamy on behalf of the MHSW. It was then forwarded to the Ministry of Justice for its approval.

A PROPOSAL FROM GERMANY

I had barely returned to New York when I received a letter from Dennis asking my opinion on a proposal for LF research from Dr Manfred Dietrich of the Bernhard Nocht Institute for Nautical and Tropical Diseases in Hamburg. Dietrich's plan was to investigate patients with fevers of unknown origin, carry out epidemiological studies of their families and contacts, conduct plasmapheresis, and investigate the effectiveness of treatment with plasma and interferon. His proposal also included the preparation of immunoglobulin. Dr Dennis asked what I thought of the proposal; he complained that everyone wanted to conduct plasmapheresis!

I responded that although the program offered more intensive study of individual patients than did mine, in many ways it duplicated what I had been proposing. I heard no more of this proposal at the time.

In the autumn of 1978, I returned to Liberia. As during the various other trips, I rented a vehicle from a missionary of the Sudan interior Mission in ELWA and visited the up-country hospitals. At CLH in Zorzor, I found a researcher, Dr J. Knobloch, of the Bernhard Nocht Institute, who had found 16 febrile patients with rising LVA titers by the IFA technique.¹⁷ Among them was a Liberian student at the Zorzor Training Institute (ZTI) nearby, and the Peace Corps nurse who had treated him. Knobloch had not been in touch with Dennis; he had entered Liberia from Sierra Leone where he had worked with the LF program of the CDC. When I returned to the ELWA radio station compound my niece told me that there was an urgent request for my presence at the US Embassy medical office, where I met with the Embassy physician and the director of the Peace Corps Mission, who were conferring on implications of the nurse's illness.

The first issue was that of how to deal with the nurse. She seemed to be convalescing well about 21 days after her illness, except for mild nystagmus and ataxia. I suggested

that her repatriation be delayed a week to avoid her isolation in quarantine and wrote a letter indicating that the longest known period of viremia had been 24 days.

The second issue was a potential political one. It appeared that within a few days, a group of new Peace Corps Volunteers were scheduled to go to the ZTI for their orientation, and the Peace Corps director wished some information regarding the LF risk there and elsewhere. He finally decided to request that the Liberian government move the program to Gbarnga, near PH. I imagined the havoc when the American Ambassador approached the unsuspecting Liberian Foreign Minister informing him of a LF outbreak in Liberia; the repercussions would echo in the Presidential palace, the MHSW and the LIBR. I drove to Dennis' home and informed him of what had happened; he then reported to the Chief Medical Officer, so that the Liberian officials were well prepared when the Peace Corps requested a change of location.

I received formal verbal notification of my proposal's approval before I left Liberia. In my exuberance I cabled my wife Veronica:

CLEO VENI VIDI VICI JULIUS.

She understood the message; she had had a classical Hungarian education.

The Honorable Kate Bryant, Minister of Health and Social Welfare, officially approved the collaborative research agreement between the Republic of Liberia and Columbia University on January 5, 1979.

Acknowledgments. The investigations cited in this article were supported in part by a gift from the Firestone Tire and Rubber Company, and Grant GA HS 7620 from the Rockefeller Foundation. The work at Yale was supported in part by Contract DADA-17-77-C 7035, the US Army Medical Research and Development Command.

REFERENCES

1. Henderson BE, Gary GW, Jr, Kissling RE, et al: Lassa fever. Virological and serological studies. *Trans Roy Soc Trop Med Hyg* 1970; 66:409-416.
2. Frame JD, Casals J: Serological testing for selected African viruses in the clinical ambience. Results of complement-fixation testing. Annual Meeting, American Society of Tropical Medicine and Hygiene, Nov 3-5, 1976. Philadelphia, PA.
3. Fraser DW, Campbell CC, Monath TP, et al: Lassa fever in the Eastern Province of Sierra Leone, 1970-1972. I: epidemiologic studies. *Amer Jour Trop Med Hyg* 1974; 23:1131-1138.
4. Letter from Robert E. Shope to John D. Frame, New Haven, CT, July 2, 1974, author's collection.
5. Letter from John D. Frame to Herta Wulff, New York City, January 2, 1975, author's collection.
6. Letter from John D. Frame to Dr Gerald A. Eddy, New York City, April 24, 1975, author's collection.
7. Letter from Gerald A. Eddy to John D. Frame, Frederick, MD, May 19, 1975, author's collection.
8. Wulff H, Lange JV: Indirect immunofluorescence for the diagnosis of Lassa virus infections. *Bull WHO* 1975; 52:429-436.
9. Frame JD: Surveillance of Lassa fever in missionaries stationed in West Africa. *Bull WHO* 1975; 52:593-598.
10. Letter from John D. Frame to J. Robert Ellis, New York City, December 11, 1975, author's collection.
11. Letter from Emmet A. Dennis to John D. Frame, Robertsfield, Liberia, March 4, 1976, author's collection.
12. Letter from Lee M. Howard to John D. Frame, Washington, DC, February 4, 1976, author's collection.
13. Letter from John D. Frame to John Maier, New York City, February 27, 1978, author's collection.
14. Letter from Betsy Brotman Liberia, to Emmet A. Dennis, Robertsfield, August 8, 1976, author's collection.
15. Utilization and supply of human blood and blood products. World Health Assembly, WHA28, 72, May 29, 1975.
16. Letter from John D. Frame to Emmet A. Dennis, New York City, May 27, 1977, author's collection.
17. Knobloch J, McCormich JB, Webb PA, et al.: Clinical observations in 42 patients with Lassa fever. *Tropen Parasit* 1980; 31:389-398.

Scientific failure in an age of optimism: Public reaction to Robert Koch's tuberculin cure

DAVID LEIBOWITZ, MD

The second half of the 19th century was a critical period in the development of modern medicine. The discoveries in the age of bacteriology provided a fundamental understanding of the nature of infectious diseases when the experiments of such men as Louis Pasteur and Robert Koch identified specific microorganisms as the causes of specific diseases. This new bacteriological revolution has been characterized as a "revolution in the knowledge of disease causation."¹ The wave of discoveries, which began in the 1860s and peaked with Koch's identification of the tubercle bacillus and cholera vibrio in the 1880s, engendered an unprecedented hope that the new knowledge concerning the causes of infectious diseases could be used to find means to prevent, treat, and even eradicate the diseases themselves. Pasteur's discovery of a treatment for hydrophobia in 1885 fueled public and medical expectations of great medical therapeutics from laboratory research. Dr William Welch of Johns Hopkins, looking back from the 1920s, recalled that "at the end of that wonderful decade, 1880-1890. . . there had been a revolution in medical thought through the discovery of the agents causing infectious disease. . . Those living today can hardly realize the enthusiasm and youthful spirit which was stirred not only among medical men, but also in the general public by these discoveries."² The stage seemed to be set for the conquest of infectious disease.

When Robert Koch announced in August 1890 that he had found a substance able to prevent the development of tubercle bacilli in humans, his finding was immediately hailed as the greatest medical discovery of the century by popular and medical periodicals alike. Within a few short months, however, the hope that a cure for tuberculosis, one of the leading killers of the day, had been found, turned to disappointment and skepticism as clinical testing revealed Koch's remedy as a failure. The rise and the fall of Koch's discovery received extensive coverage in the popular press and the dashed hopes the "cure" left behind deeply shook the public's optimism regarding the possibilities of bacteriology. Paul Starr called Koch's failure "a severe reverse in the clinical application of bacteriology;" later bacteriological work had to overcome the popular skepticism created by Koch's failure to regain its previous widespread acceptance among the public.³

Although the bacteriological discoveries of the late 19th century have been well documented by physicians and medical historians such as Richard Shyrock, Paul De Kruif, Elie Metchnikoff, and others, the reaction of the public to

these discoveries has not been studied as thoroughly. An examination of the press coverage of Koch's cure shows how the extensive coverage of this medical failure affected public reaction to the next great bacteriological innovation, the introduction of diphtheria antitoxin in 1894.

In attempting to determine public opinion concerning Koch's cure and its aftermath, it is important to recognize the impact of the new communications technology of that time which greatly facilitated the mass production of newspapers and the relatively rapid transmission of news from abroad. The number of daily papers doubled in the 1870s, and the years 1880-1900 have been called the "Golden Age of Journalism."⁴ These technological innovations were matched by the movement of most newspapers away from close relationships with political parties and toward a more independent, fact-oriented journalism. This new attention to information and entertainment rather than political leadership led newspapers to become much more attuned to public opinion and popular interests. Smith, in his noted history of journalism, has observed that newspapers could now claim to be representative of large segments of opinion.^{4(p43)} Because the press was able to "conjure with the moods and minds of its massed readers"^{4(p161)} in this period, it provides an excellent source for the study of popular opinion.

EARLY SUCCESSES

Robert Koch, born in 1843 in central Germany, studied medicine at the University of Gottingen where he graduated at the age of 19. His first major bacteriologic discovery was the isolation of the anthrax bacillus in 1876. This was followed by his crowning achievement, the isolation of the tubercle bacillus in 1882. In 1884, Koch identified the cholera vibrio and published his famous postulates, rules governing the link between infection and disease in force to this day. Koch's work before 1890 received some coverage in the media, and his name was familiar to the public. Koch's discovery of the tubercle bacillus in March 1882 was the subject of two articles and an editorial in May of that year in the *New York Times*. In the first article, dated May 3, a dispatch from the *London Times* was printed, describing in detail Koch's experiments with the bacillus.⁵ Two days later, a *New York Times* editorial proclaimed, "A learned German scientific person has just made what is heralded by the press as a grand discovery. . . Professor Koch is inclined to think that a remedy for tuberculous consumption is possible in a process analogous to vaccination."⁶ Thus as early as 1882, Koch's name was connected in the media to a possible cure for tuberculosis. In July 1884, after Koch's discovery of the cholera vibrio, the *New York Times* ran a

Address correspondence to Dr Leibowitz, 760 W End Ave, Apt 7A, New York, NY 10025.

biographical sketch of Koch, "whose name is at present on everybody's mouth appears." The article closed with the statement that "although the Germans call him theirs with pride, he will remain always what he is, universal, and he deserves to the full the honorable title of benefactor of humanity."⁷ This early coverage of Koch's work illustrates how great an interest the media was already developing in bacteriology.

Pasteur's discovery of a cure for hydrophobia in 1885 attracted far more press attention. In a lecture delivered at the Pasteur Institute in Paris at a colloquium celebrating the 100th anniversary of the Institute, Dr Bert Hansen of New York University claimed that this was the first time that a medical advance had been treated by the popular press as a sensational news item (unpublished). In December 1885 and January 1886 alone over 30 different articles concerning the rabies cure appeared in both the *Times* and the *Herald*, several of which received front-page headlines. The major aspect of the story covered by the press was the account of the Newark children who, after being bitten by a mad dog, travelled to Paris for treatment by Pasteur. Pasteur's name rarely appeared in print without adjectives such as "genius" or "savant" attached to it. This image, propagated in the press, of hopeless people travelling from around the world to seek out a scientific genius for treatment of a terrible disease, helped increase public expectations that laboratory research would soon be able to cure the killer diseases it had done so much to understand.

KOCH'S ANNOUNCEMENT

In August 1890 at the 10th International Medical Congress in Berlin, Robert Koch announced that he had found substances "which both in the test tube and in the living body prevent the development of tubercle bacilli."⁸ Although Koch admitted his experiments were incomplete, his words, coming from such an accomplished scientist, created high expectations at the Congress. In the words of Dr Paul Gibier, director of the New York City Pasteur Institute, "All the experimenters that I met at the Congress were of one opinion. We agreed . . . that from the moment Koch communicated a fact of such great importance, that fact must exist."⁹ Elie Metchnikoff claimed that those attending the Congress were convinced that Koch had succeeded in his quest for a cure of tuberculosis and that his subsequent communications on the matter were anticipated with great interest.⁸ Although Koch's statements at the Congress attracted medical attention, it does not appear that any of his claims found their way into the lay press.

Several months later, in an article entitled, "Further Communication Regarding a Remedy for Tuberculosis," published in the *British Medical Journal* of November 15, 1890, Koch fully explained the effects his remedy could have on cases of tuberculosis (Fig 1).¹⁰ He stated that the remedy, did not kill the bacilli themselves but instead caused necrosis of living tubercular tissue. Koch affirmed that incipient cases could be cured "with certainty" by the remedy, but he warned that chances of success were far smaller in advanced cases. Koch made clear his opposition to indiscriminate application of the remedy and claimed that he needed to do further testing before more definitive statements could be made. Koch said he felt it necessary to publish now to prevent the spreading of false ideas on the subject. Koch did not reveal the exact nature of his remedy in this first report, an omission that would result in much



FIGURE 1. This illustration taken from *Leslie's Illustrated Newspaper* hailed Koch as the discoverer of the cure (reprinted from *Leslie's Illustrated Newspaper* 71: December 13, 1890, p 349).

criticism in the weeks to come. In this paper, the remedy was simply described as a "brownish, transparent fluid;" Koch reserved elaboration for a future communication.

Unlike Koch's statements in August at the Congress, the appearance of his report in November created an immediate media sensation. On November 15, the *Times* ran a front-page headline entitled "The Foe of Tuberculosis" with an accompanying article that was a full translation of Koch's article from the *Deutsche Medizinische Wochenschrift*, obviously believing that not only the content but the medical journal article itself was worthy of front-page coverage in a lay newspaper.¹¹ The next day the *Times* contained another front-page article titled "Koch's Great Triumph." The article began with the simple statement "Prof Koch holds supreme sway over public interest" and went on to describe the enthusiastic reception the remedy received from most of the medical world. The piece quoted Professor Nothnagel of Vienna University addressing his students, "We face one of the greatest intellectual achievements in medicine for centuries past. Prof Koch's discovery has a far wider scope than Jenner's and is perhaps the grandest feat in the history of our science. . . The present moment is among the most sublime that humanity has ever known." Uproarious applause is said to have followed the lecture.¹² This statement is typical of the rhetoric surrounding Koch's cure in the first week after its disclosure, rhetoric that covered the front pages of mass newspapers all over the United States.

It has been claimed that New York physicians did not share the enthusiasm generated by Koch's triumph.¹³ How-

ever, a *Times* article on November 17 presented the first interviews with local physicians whose “great interest and speculation” had naturally been aroused.¹⁴ Similarly, the *World* reported several days later that “there is great rivalry among the doctors of the city and Brooklyn to be the first to get information from Dr Koch regarding his new discovery.”¹⁵ Although the practitioners generally expressed a conservative attitude, Koch’s first-rate reputation as a scientist led many to immediate optimism. Dr E. Trudeau stated that “Dr Koch discovered the tubercle bacillus nine years ago and pointed out that it was the cause of consumption. . . . When after years of silence he now tells us that he has found a remedy which not only prevents but cures consumption at any rate in its earlier stages and simpler forms, the utmost interest must be felt.”¹⁴ Dr T. Mitchell Prudden, Professor at Columbia and member of the New York City Board of Health, was reported in the same article as endorsing Dr Trudeau’s views.¹⁴ All the New York papers reported on the plans of Dr Abraham Jacobi, a prominent city physician and ex-president of the New York Academy of Medicine, to obtain the lymph for use at the Mount Sinai Hospital.¹⁶ The *World* reported that a group of city physicians headed by Dr H. Curtis sailed to Berlin to study Koch’s treatment and planned to open a sanitarium in New York using Koch’s methods.¹⁷

Coverage of the “great discovery” was not confined to the *Times*. A *Herald* article on November 17 entitled “A Great Discovery Say N.Y. Doctors” quoted Herman Biggs, member of the Board of Health and a man who would eventually become State Commissioner of Health, as saying “From Koch any statements must be received with much confidence.”¹⁸ On the 18th, the *Commercial* quoted Dr Prudden, who said, “Dr Koch is such a careful worker, there seems little reason to doubt.”¹⁹ The fact that the name of such a universally recognized scientist was linked to the new cure gave it instant credibility to these local doctors as well as the public (Fig 2).

The excitement over the cure continued over the next few days as the press coverage remained intense. News of the cure spread so fast that by November 20th, the *Herald* was already warning American consumptives not to travel to Berlin for treatment because of the crowds and the shortage of lymph there.²⁰ Even the cautious Dr Koch was swept up in the enthusiasm. During an interview with the *New York Sun* Koch held up a vial of his precious fluid and exclaimed, “I believe I have it here!”²¹ The media adopted religious themes and there are many references to foreign doctors and patients converging on Berlin as “pilgrims” flocking to “Mecca.”²² News of the cure travelled so far so fast that by November 22, the *Times* reported cables from Australia arriving in Berlin requesting lymph to be sent for treatment.²³

Leading American medical journals were also enthusiastic about Koch’s announcement. The *Medical Record*, edited by Dr George Shrady, proclaimed, “The imagination cannot fail to be impressed by the possibilities apparently opened up by Koch. . . . Medicine can hold up its head as a science and defy with confidence all the jeers that may be thrown at its inefficacy.” In a foreshadowing of what was to come, the editorial closed on a cautionary note, warning, “We hope all which Koch promises will be fulfilled, it would be a profound catastrophe to medical science if he should fail.”²⁴ The *Record* sent Dr Max Einhorn, an ex-pupil of Koch’s to Berlin to report firsthand on progress being made. In addition, the *Record* published a special supple-



FIGURE 2. Taken from a Berlin newspaper of the period, this print is typical of the adulation Koch received following the announcement of his cure (reprinted from *Review of Reviews* 2(20): December, 1890, p 527).

ment to its December 13 edition written by Koch explaining in detail his method of treating tuberculosis.²⁵

The *New York Medical Journal*, edited by Frank Foster, MD, took a far more critical stance than other medical journals of the time, as evidenced by the title of its first editorial on the subject, “Koch’s Alleged Cure For Tuberculosis.” Foster was critical of what he considered Koch’s premature publication of his cure and felt that the press sensation surrounding the cure was distorting the medical reality. In spite of this attitude, even Foster was swayed by Koch’s scientific reputation and stated “. . . so great his name—so great his genius—that any observation of his carried with it a universally admitted probability of truth.”²⁶

PREVALENCE OF TUBERCULOSIS

To understand the sensation that this supposed cure for tuberculosis created, it is important to keep in mind how prevalent the disease was at the time of Koch’s announcement. Tuberculosis (TB) had replaced smallpox as the scourge of Europe and was referred to as the “white plague.” In 1890, TB caused 10%–15% of all deaths in Europe, and for the 15–60 age group in Germany this percentage rose to one third of all deaths. The annual death rate from TB on the east coast of the US, combining the statistics from Boston, New York, and Philadelphia, was between 300 to 400 deaths per 100,000 total population for the period.²⁷ Unlike most infectious diseases, TB has a slow and insidious spread through the body, in some cases causing years of debilitation and misery. No effective drug therapy had ever been found, although many different types of drugs were prescribed for its treatment. A physician, writing some 40 years later recalled that some of the more

popular regimens included cod-liver oil, tartar emetic, digitalis, and even opium. Many new remedies for any disease were immediately tested for their efficacy against TB.^{27(p150)} In the middle of the 18th century, the therapeutic value of rest gained prominence in the treatment of tuberculosis, and the 19th century saw the development of the closed sanitarium. Rest at high altitudes in locations with temperate climates and lots of sunshine was the primary therapy for tuberculosis at the time of Koch's discovery. Since there was no real cure for tuberculosis, the excitement among consumptives created by the announcement of Koch's cure does not come as much of a surprise. What does is the degree to which the popular press perceived the announcement of a cure as a newsworthy event, deserving of priority coverage for weeks on end.

THE CONTROVERSY

As coverage of the cure continued through the end of November, the first criticisms of Koch appeared when clinical testing began to show that the cure was not particularly effective. Already in late November, the *Times* had reported that, "though confidence in the ultimate value of Prof Koch's discovery does not abate, disappointment over public trials grows daily."²⁸ The *Herald* that day mentioned the same growing discontent and said that, "Dr Koch blames the press for raising hopes of instant benefit in every form of tuberculosis."²⁹ An indication of the change in climate from the euphoria that first surrounded his announcement was Koch's interview with the *World* on December 23, sharply contrasting with the interview given in the *Sun* a few days before. In this interview, Koch was described as being reluctant to talk, and faced with growing criticism, claimed he was forced to reveal his cure prematurely because of pressure after his statements in Berlin in August.³⁰ This theme of premature publicity was echoed by Dr Prudden in an interview with the *Herald* November 23 in which Prudden also seemed to have lost some of his early enthusiasm concerning the cure. Prudden stated, "Koch does not claim that all cases of consumption will be cured or even benefited by the remedy" and that it was still unclear how useful the remedy would be.³¹

In spite of these early negative reports, Koch continued to receive strong support in editorials, a good indicator of public opinion. On November 19, the *Herald* said, "most eminent physicians who have spoken, while properly deferring final judgement, seem inclined to freely admit that Prof Koch's work inaugurates a new bright era in the treatment of consumption and all diseases dependent on pathogenic microorganisms."³² In a *World* editorial on the November 23, the editors claimed that any new ideas meet with hostility and pointed to Jenner's vaccine for smallpox and Pasteur's for hydrophobia as examples of medical discoveries originally greeted with hostility in the medical community. The editorial closed by saying of Koch, "there is no name on the roll which will equal his."³³

The next few weeks were ones of growing medical controversy regarding the possibilities of Koch's therapy, with conflicting medical reports concerning its efficacy appearing almost daily in the news reports. The scientific controversy did not dampen the press' enthusiasm, particularly as the early reports were mostly favorable. Koch's reputation as a great scientist continued to influence physicians, and magazines such as *Harper's Weekly* and *Leslie's Illustrated Newspaper* contained illustrations of Koch and his laboratory as Koch temporarily replaced Pasteur as

the "true savant." *Leslie's* even raised funds to send a consumptive to Berlin to receive the new treatment (Fig 3).³⁴

Two items in mid-December particularly reveal how pervasive news of Koch's cure had become. The headline of an advertisement for Soden Mineral Pastilles in the *Times* on December 14 claimed that "Sir Morell Mackenzie experimented with Koch's lymph," this being the same Sir Morell Mackenzie whose testimonial appeared on each box of the Pastilles, used for "catarrh, sore throat, coughs, and all throat and lung diseases."³⁵ The mere mention of Koch's lymph was considered by this advertiser as the best way to both catch the public's eye and help legitimize their product, an indication of how widespread the coverage of Koch's cure was. In the December 10 issue of *Puck Magazine*, a weekly satirical magazine, published in New York, a double page cartoon showed a dying elephant with a Republican party figure injecting it with a large needle with the sign "reciprocity lymph." The cartoon was captioned "A Bad Case of Consumption—Dr Blaine Tries An Injection of His Reciprocity Lymph."³⁶ Obviously, the cartoonist felt that image of the consumption cure was well-known enough for it to convey a political message (Fig 4).

THE CONTROVERSY CONTINUES

As further clinical work began to cast doubt on the efficacy of the lymph, two events of mid-January proved to be major turning points in both medical judgment and popular opinion toward Koch's remedy. On January 7, Rudolf Virchow delivered his review of 21 necropsy findings of patients treated with the remedy to the Berlin Medical Society. Virchow observed that use of the lymph actually facilitated the spread of the bacilli from the original tubercular nodules thus hastening the death of the consumptives on whom the lymph was tried. This observation, coming from a man then regarded as the "main arbiter of international medicine"³⁷ who had earlier defended Koch against his critics, had a major effect on medical and public opinion.³⁸ Finally, a scientist whose scientific, if not popular reputation was equal to that of Koch had opposed the use of the remedy. The *British Medical Journal* reported from Berlin that Virchow's findings "seem to be almost a death knell for the lymph."³⁹



FIGURE 3. An illustration from *Leslie's Illustrated Newspaper* depicting the Koch treatment for consumption given by Prof Ewald at the Augusta Hospital in Berlin to a patient sent by the newspaper (reprinted from *Leslie's Illustrated Newspaper* 7134(p408)).



FIGURE 4. Cartoon entitled "A Bad Case of Consumption—Blaine Tries an Injection of Reciprocity Lymph," (reprinted from *Puck Magazine* 23⁶).

This new medical information was rapidly reported in the press. The *Times* noted the story on January 15 when an article proclaimed "The Lymph Very Uncertain." This latter article discussed Virchow's autopsies and said that "post-mortems show (the lymph) is dangerous in many cases."⁴⁰ The *Times* followed with a front-page story in the January 18 issue entitled "Prof Koch's Many Critics," the first occasion an article critical of Koch had appeared in such a prominent location.⁴¹ In an editorial the next day, the *Times* claimed "there is a steadily growing impression that the so-called lymph discovered by Prof Koch should be used with great caution. This impression is deepened by the reports of Virchow."⁴²

On January 14, 1891, one week after Virchow's critical report and two months after Koch's original communication, Koch disclosed that his heretofore secret remedy was a "glycerine extract of a pure cultivation of the tubercle bacilli," a substance to become known as tuberculin. This announcement came as a great disappointment to the medical world, which had eagerly anticipated Koch's description of his secret remedy. At least one model had been developed by physicians to understand how to cope with infectious diseases. It was known that Pasteur's hydrophobia vaccine involved the use of an attenuated form of the disease-causing virus itself that stimulated the body's defenses without causing the disease itself. Although the question of how widespread this knowledge was by January 1891 has not been researched, in the months previous to Koch's announcement of a tuberculosis cure, workers in Koch's laboratory discovered diphtheria and tetanus antitoxins understood to be substances produced by the body in response to an infectious agent. Koch's vague "glycerine extract" seemed to fit neither of these models of cures, which were quite immunologically specific and the general nature of his statement led many physicians and prominent medical journals including the *Medical Record* and the *New York Medical Journal* to further questioning of the effectiveness of his remedy.

As in the case of Virchow's post-mortems, medical disappointment immediately received attention in the press. In a report on January 16, the *Times* translated Koch's explanation of his remedy and followed Koch's explanation with the criticisms of many doctors who felt it was insufficient.⁴³ Physicians had wanted Koch to explain both how the remedy worked and how it could be produced so that

they would no longer have to rely on supplies from Germany. Koch's disclosures satisfied neither of these concerns and physicians were no longer willing to give Koch the benefit of the doubt. The *Post* and the *Herald* also carried Koch's report. The *Herald* defied most medical opinion, stating in an editorial that same day, "the revelation which Prof Koch now makes will immensely raise the confidence of his scientific physicians in the future therapeutic value of his cure despite the recent unconfirmed criticism of Prof Virchow."⁴⁴

News coverage of Koch's cure sharply dropped after mid-January, evidence that Virchow's criticism and Koch's disappointing announcement concerning the nature of the lymph were major turning points in the episode. After two months of almost daily reports since November, coverage in the *Times* dropped abruptly. The *Times* exhibited a very swift transition in its coverage of the cure, from daily reports on the discovery of the century to periodic reports of a continuous failure. This transition must have had quite an impact on a public which had been subjected to barrages of news reports for two months (Fig 5).

Over the next six months, the lymph was mentioned every few weeks in articles of a paragraph or two which usually reported the abandonment of the treatment in a particular city. By July, the reputations of Koch and his remedy had fallen so far that the *Times* could report on the 24th that Koch had resigned all public offices he held, a step "associated with supposed disappointment over the unsatisfactory results of his discovery of tuberculin."⁴⁵ On the 26th, the *Times* corrected its story, saying its previous report was a false rumor and that Koch's resignations were not due to the failure of his cure but because he was

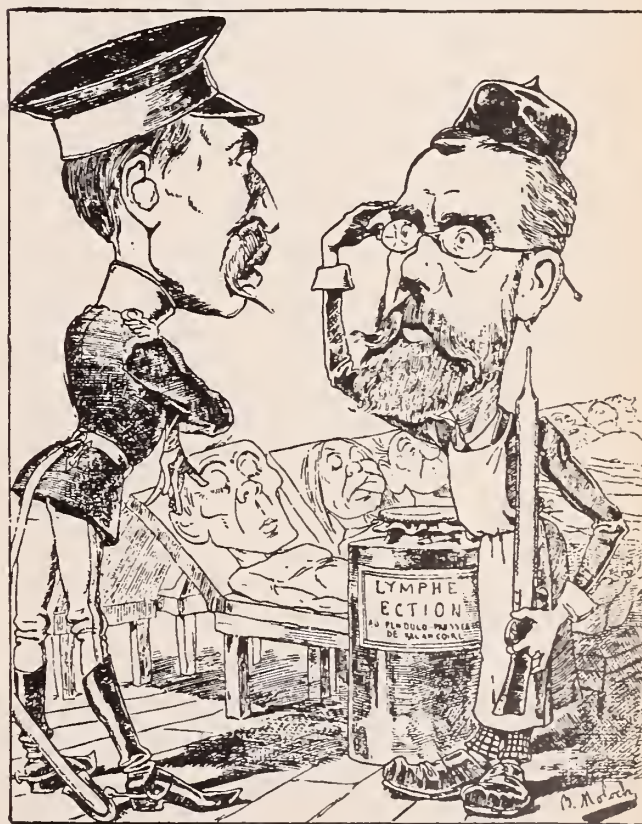


FIGURE 5. This cartoon shows the extent of public ridicule of Koch after the failure of his cure (reprinted from *Review of Reviews* 3(2): February, 1891).

assuming a new office, that of Director of the Institute for Infectious Diseases, all of which was true.⁴⁶ On July 28, a full column article, the last solely concerned with the lymph to appear in the *Times* proclaimed "Lymph Called a Failure."⁴⁷ It was printed by the *Times* after a statement from Berlin that Koch had ended his researches on tuberculosis. The article reported that in New York only one patient was still undergoing treatment, where formerly there were hundreds, a statistic cited by the writer as proof of the "complete failure" of the lymph. All of the physicians who had been running trials except one reported that they had completely ended their use of the lymph.

The January news of Virchow's findings and Koch's second report had an effect even on the coverage of the optimistic *Herald*. The decline in the amount of coverage of the lymph and the increasing negativism of articles which did appear from February on are even more apparent in the *Herald* than in the *Times* when one considers the former optimism of the *Herald* regarding the cure. An article on February 6 entitled "Severe on Koch's Lymph" contained the negative opinions of several European physicians.⁴⁸ On February 12, a small paragraph reported the opening of the Koch Institute on East Broadway under the direction of Dr Aaronson.⁴⁹ The Institute, built to accommodate 40 patients contained only ten. By February 22, a *Herald* reporter said in "What the Doctors Say," a weekly feature, "I thought it would scarcely be necessary to refer again to Dr Koch's remedy, if the name remedy can be given to a means which in the majority of cases, renders worse than the complaint it is meant to cure. . . ."⁵⁰ On the next day, February 23, an article proclaimed "Professor Koch's Lymph A Disappointment" and quoted Dr George Shrady, founder and editor of the *Medical Record*, and others active in the clinical testing of the lymph in New York City, who all gave very negative appraisals of the lymph.⁵¹ The editors of the *Herald*, who had initially maintained interest in the cure even after the reports of Virchow and Koch, were now resigned to the lymph's failure. Koch's resignations and appointment at the end of July, covered in the *Times*, are not mentioned in the *Herald*. Once it was apparent that the lymph was a failure, the *Herald* lost interest in the story.

For the period covered by this paper, it appears that Koch's tuberculin did not become accepted in clinical practice as a therapeutic agent for tuberculosis. Although the early enthusiasm of the public surrounding Koch's tuberculin had turned to widespread disillusionment, scientists continued to experiment with the cure out of the public eye. The diagnostic value of tuberculin was recognized very quickly and many attempts were made to develop and test different types of tuberculin for therapeutic use even after Koch's failure. Dr E. Trudeau, the famous New York physician and founder of the Saranac Lake sanatorium, experimented with it until his death in 1915.⁵² Koch himself maintained his faith in tuberculin as a possible cure for tuberculosis and as late as 1894 criticized those doctors who had not availed themselves of its use.^{8(p122)}

REPERCUSSIONS

The sensation caused by Koch's discovery was recognized by contemporaries as being unparalleled in history. Dr Nicholas Senn, writing in the *Medical News* in June 1891 said, "For days and weeks the public press devoted a liberal space to telegraphic messages, to editorials and messages from medical men, relative to the new treatment. . . . No other event in the world's history ever attracted so much

attention and no discovery in medicine and surgery ever found such ready introduction and universal acceptance."⁵³ A biographer of Koch, who was in medical school in the US at the time of Koch's original announcement, wrote almost 50 years later, "I can well recall the excitement produced in the world and the hopes aroused in consumptive patients."⁵⁴

The great publicity concerning Koch's cure and the widespread public disappointment after its failure caused a severe setback in public optimism toward bacteriological innovation. This effect of Koch's failure becomes evident in an examination of the press reaction to the introduction of diphtheria antitoxin in 1894, which is treated at length in Terra Ziporyn's *Disease in the Popular American Press*.⁵⁵ The introduction of antitoxin is a useful example with which to study the effects of the tuberculin fiasco on public opinion of bacteriology because it was the first major bacteriological discovery introduced after the Koch incident. Furthermore, at least part of the credit for the development of the antitoxin belonged to the same German laboratory that produced Koch's tuberculin (although, as we shall see, this credit was rarely forthcoming). Press coverage of the antitoxin shows that the image of Koch's failed lymph and still strong in American consciousness in 1894 and that this image strongly conditioned how the press, and thus the public, reacted to the introduction of antitoxin.

The exact effect that Koch's lymph disaster had on those active in bacteriological research is an intriguing one, but one that is outside the scope of this paper. The fiasco probably reaffirmed the need for cautious experimentation and the avoidance of uncontrolled publicity. Dr A. S. Coe, in a lecture printed in the *New York Medical Journal* in 1891 stated that "this wild enthusiasm which greeted the announcement of the tubercular cure is a fitting commentary on the credibility which too often accepts conclusions without adequate investigations or proof. This failure and revulsion, because of disappointment, will have a salutary influence. It will divert attention from the lab. . . to the study of the more complex vital forces, which underlie it. . . ."⁵⁶ The delay in the use of diphtheria antitoxin, first developed in December 1890 and first used clinically in the winter of 1891-1892 provides some evidence for this. When the results of the experiments using diphtheria antitoxin were finally divulged in August 1894, one reason for the prolonged secrecy given by Dr Cyrus Edson, Medical Commissioner of the New York Board of Health, was "the fiasco of the famous 'lymph' treatment of consumption, which was made public before the experiments had been concluded."⁵⁷

During the interval between the tuberculin fiasco and the introduction of diphtheria antitoxin in 1894, little mention was made of Koch in the popular press. An editorial in the *Times* dated June 26, 1892, referred to a scandal in Berlin caused by Koch's private life. This scandal, the *Times* said, "has brought back the name of Herr Robert Koch, the Gelehrter who thought he had tracked to its lair the bacillus of consumption and knew how to slay same. The excitement of the whole world over this supposed discovery. . . was followed by a neglect as profound as the interest in Herr Koch was before." The *Times* suggested that the "deserted savant" had "consoled himself for the fickleness of the public by running off with a dancer." The article closed by saying, "Yet of Koch's services to science there can hardly be a question."⁵⁸ Although the *Times* recognized Koch's early scientific contributions, the great scientist is now seen

as a deserted genius, his reputation ruined by the failure of his cure for tuberculosis. A small article appeared in the *Times* on May 16, 1893, again on Koch's domestic scandal.⁵⁹ It is interesting that the only references to Koch in this period concern his private life and not his scientific researches in spite of the fact that in his laboratory substantial progress on diphtheria and tetanus antitoxin was being made. Although much of this laboratory work was kept secret, a few articles did appear, but made no mention of Koch's involvement. As Dr E. Trudeau stated in a paper presented to the Association of American Physicians in May 1893 "the gigantic human experiment which followed (Koch's announcement) and resulted in so much inevitable disappointment is still fresh in the public as well as professional mind."⁶⁰

LESSONS LEARNED

The first story in the New York popular press on the new treatment for diphtheria was a *Times* editorial on August 24, 1894, the day after Dr Herman Biggs reported on the antitoxin to the New York City Board of Health upon his return from Europe.⁶¹ The editorial was supportive of the new cure and relied heavily on the assurance of Dr Edison, who was described as a "sensible and cautious" physician. On August 27, the *Times* contained an article entitled "Sure Cure For Diphtheria."⁶² Although Koch was immediately given credit for the discovery in the subtitle, "Dr Koch Its Discoverer and Antitoxin Its Name," the evidence favoring its use was that presented by local officials, Edson and Biggs, who, even at this early date in their careers, were highly respected by the press and public.⁶³ That same week reports on the diphtheria cure appeared in both the *Tribune* and *Herald*. The *Tribune*, in its report on August 26, tried to counter some of the popular skepticism it expected by blaming Koch's failure on his cure's inappropriate use by "charlatans."⁶⁴ The article called for antitoxin to be introduced under the direction of sanitary authorities and claimed, "This warning is particularly necessary since great harm was caused by the unscientific use of Dr Koch's previous investigations regarding consumption." This claim, that the failure of Koch's consumption cure was the result of its unauthorized use by unqualified people, which was to reappear in later press reports is not supported by any real evidence. No mention of this charge was made by the press in the months when Koch's cure was failing. The reason then given was the disappointing clinical results and the subsequent disillusionment of many physicians. Perhaps the *Tribune* attempted to defuse public skepticism by using "charlatans," as scapegoats for the failure of Koch's lymph.

The press response to the introduction of antitoxin in late August was very cautious and placed a heavy emphasis on reporting statistics and case reports. This restraint stood in great contrast to the media's immediate acceptance of Koch's cure before any real evidence was obtained. The statistics and cases first quoted in the August articles continued to appear in the *Times* over the next several months. In addition, the press coverage of the diphtheria cure that occurred always sought to distinguish antitoxin and tuberculin clearly. This differentiation was accomplished in many different ways. A *New York Times* editorial on September 6, which expressed confidence in the remedy, tried distinguishing between the physical properties of antitoxin and the discredited tuberculin. The *Times* explained, "Prof Koch's tuberculin is a reduced culture of the bacillus of tuberculosis and it is now held we think, by

certain authorities that in administering it to tuberculosis persons poison was added to poison. . . ." Antitoxin on the other hand was "something that is harmless," not a culture of the diphtheria germ.⁶⁵ Another *Times* editorial on September 20 emphasized that the antitoxin was unrelated to the diphtheria poison but was a "substance which is hostile to that poison and its most powerful enemy."⁶⁶ The editorial stated that the public should realize that only something related to the poison of the bacillus itself, such as Koch's tuberculin, could accelerate the disease process.

The *Herald* also attempted to make clear to its readers that the antitoxin cure was different than tuberculin. The ways the *Herald* tried to make the distinction are particularly informative since the paper began a public subscription drive aimed at raising money for the production of antitoxin by the Board of Health on December 10, 1894.⁶⁶ Headline stories about diphtheria antitoxin and the campaign were featured until the end of December and the drive itself continued until the fall of 1895. This campaign was aimed at the general public and an examination of the coverage reveals the need the *Herald* felt to try to overcome the public's skepticism, skepticism created by the failure of Koch's lymph.

Local health officials were given the task of convincing the public that the antitoxin was worth their money and to do so, they felt the need in their comments to explain why the antitoxin was different from tuberculin. Unlike the August articles in the *Times*, emphasizing the chemical differences between the two cures, these reports emphasized the completeness of the clinical trials of the antitoxin and the near unanimity of medical opinion concerning the efficacy of the antitoxin. For example, on December 10, Dr H. Curtis stated that "Unlike Koch's lymph, the diphtheria antitoxin has withstood the severest tests." Later in that article, the point is made that "we have medical men from all over the world, from none of these doctors have we heard a single criticism."⁶⁷ The next day Dr R. Dormus said "I do not apprehend any disappointment as in the case of Koch's lymph, for I consider that Dr Roux's trials have been complete and convincing."⁶⁸ One physician claimed that Rudolf Virchow, whose opposition to the lymph hastened its downfall, supported the antitoxin, evidently hoping that Virchow's support would help the antitoxin in the same way that his opposition hurt the tuberculin cure.⁶⁹ The few doctors cited by the *Herald* as being undecided or even negative inevitably cite Koch's lymph as support for their own conclusions. An example of this attitude is Dr G. Hope who said on December 12, "You see I am in some points a doubter of the efficacy of these discoveries. They begin by curing everything and end in losing all virtue. There was Koch's lymph for example!"⁷⁰ Four years later, the image of Koch's failed lymph clearly influenced the minds of physicians and the public.

CONCLUSIONS

The public reaction to Koch's tuberculin must be seen in the context of the bacteriological discoveries of that time period. The discoveries of the 1880s, such as Koch's identification of the tubercle bacillus and Pasteur's vaccine for hydrophobia, created great and perhaps unrealistic expectations among the medical world and the general public, both of which looked toward the imminent demise of infectious disease. When Koch, a man recognized as a scientific genius by physician and layman alike, announced his cure for tuberculosis in 1890, the public leapt to embrace it,

disregarding any pleas for caution or restraint. This is a revealing tale of the consequences of releasing medical innovations to the public before proper clinical investigation and peer review, a tale that has unfortunately been repeated many times in the century since Koch's announcement. The public and scientific disillusionment with Koch's cure was a major setback to the newly emerging science of bacteriology, a setback that should have been avoided. Although physicians and public of the time learned a healthy skepticism from Koch's debacle, the issues raised by this incident remain with us today. In an era, when leading physicians and journals are facing intense pressures from the media and lay organizations to release scientific data before proper peer review, the lessons of Koch's lymph are particularly relevant.

REFERENCES

1. Shyrock RH: *The Development of Modern Medicine*, Philadelphia, University of Pennsylvania Press, 1936, p 240.
2. Winslow CE-A: *The Life of Herman Biggs*, Philadelphia, Lea and Febiger, 1929, p 78.
3. Starr P: *The Social Transformation of American Medicine*, New York, Basic Books, 1982, p 138.
4. Smith A: *The Newspaper. An International History*, London, Thames and Hudson, 1979, p 43.
5. Tyndall on Koch's work, *NY Times* May 3, 1882, p 2.
6. New Parasites, *NY Times* May 5, 1882, p 4.
7. Dr Robert Koch, *NY Times* July 7, 1884, p 5.
8. Metchnikoff E: *The Founders of Modern Medicine*, NY, Walden, 1939, p 72.
9. Gibier P: Dr Koch's Discovery, *N Amer Rev* 1890; 151:728.
10. Koch R: Further communication regarding a cure for tuberculosis, *Brit Med J* 1890; 2:1193.
11. The foe of tuberculosis, *NY Times* November 15, 1890, p 1.
12. Koch's great triumph, *NY Times* November 16, 1890, p 1.
13. Fox D: Social policy and city politics. Tuberculosis reporting in New York, 1889-1900, *Bull Hist Med* 1975; 49:169-195.
14. Koch's curative lymph, *NY Times* November 17, 1890, p 3.
15. Will test the lymph, *NY World* November 20, 1890, p 3.
16. How he got the lymph, *NY World* November 24, 1890, p 4.
17. Invitations to Berlin, *NY World* November 21, 1890, p 3.
18. A great discovery say New York doctors, *NY Herald* November 17, 1890, p 12.
19. Koch's cure, *NY Commercial* November 18, 1890, p 4.
20. The tuberculosis cure, *NY Herald* November 20, 1890, p 7.
21. An interview with Koch, *NY Sun* November 21, 1890, p 4.
22. Like pilgrims to Mecca, *NY World* November 17, 1890, p 3.
23. Hospitals for Koch, *NY Times* November 22, 1890, p 5.
24. Koch's cure for tuberculosis. *Med Rec* 1890; 38:579.
25. The inoculation method of treating tuberculous disease. *Med Rec* 1890; 38:suppl.
26. Koch's alleged cure for tuberculosis, *NY Med J* 1890; 52:570.
27. Webb GB: *Tuberculosis*, New York, PB Hoeber, 1936, p 13.
28. A decoration for Koch, *NY Times* November 23, 1890, p 3.
29. Dr Koch's remedy, *NY Herald* November 23, 1890, p 19.
30. A talk with Dr Koch, *NY World* November 23, 1890, p 1.
31. What Dr Koch has found out, *NY Herald* November 23, 1890, p 27.
32. Prof Koch's critics, *NY Herald* November 19, 1890, p 8.
33. The consumption cure, *NY World* November 23, 1890, p 3.
34. Dr Koch's treatment, *Leslie's Illustrated Newspaper* 1891; 71:405.
35. *NY Times* December 14, 1890, p 3.
36. A bad case of consumption, *Puck* 1890; 2:276-277.
37. Ackerknecht EH: *Rudolf Virchow. Doctor, statesman, anthropologist*, Madison, University of Wisconsin Press, 1953, p 27.
38. Invitations to Berlin, *NY World* November 21, 1890, p 3.
39. Reports from Berlin. *Brit Med J* 1891; 1:132.
40. The lymph very uncertain, *NY Times* January 15, 1891, p 3.
41. Prof Koch's many critics, *NY Times* January 18, 1891, p 1.
42. Prof Koch's discovery, *NY Times* January 19, 1891, p 4.
43. The secret of the lymph, *NY Times* January 16, 1891, p 1.
44. Koch's lymph is unveiled, *NY Herald* January 16, 1891, p 6.
45. Prof Koch's disappointment, *NY Times* July 24, 1891, p 4.
46. Koch has a new office, *NY Times* July 26, 1891, p 4.
47. Lymph called a failure, *NY Times* July 28, 1891, p 8.
48. Severe on Koch's lymph, *NY Herald* February 6, 1891, p 7.
49. The new Koch Institute, *NY Herald* February 12, 1891, p 21.
50. What the doctors say, *NY Herald* February 22, 1891, p 21.
51. Prof Koch's lymph a disappointment, *NY Herald* February 23, 1891, p 4.
52. Caldwell M: *The Last Crusade*, New York, Atheneum Press, 1988, p 167.
53. Senn N: Away with Koch's lymph. *Med News* 1891; 58:625.
54. Webb GB: R. K., *Ann Med Hist* 1932; 4:509-523.
55. Ziporyn T: *Disease in the Popular American Press. The Case of Diphtheria, Typhoid Fever, and Syphilis, 1870-1920*, New York, Greenwood Press, 1988, p 32.
56. Coe AJ: Therapeutics, *NY Med J* 1891; 54:239.
57. Sure cure for diphtheria, *NY Times* August 27, 1894, p 1.
58. Brown-Sequard again, *NY Times* June 26, 1892, p 4.
59. Professor Koch domestic scandal, *NY Times* May 16, 1893, p 7.
60. Trudeau E: *The Treatment of Experimental Tuberculosis by Koch's Tuberculin*, Philadelphia, 1892.
61. *NY Times* August 24, 1894, p 4.
62. Duffy J: *A History of Public Health in New York City*, New York, Russell Sage Foundation, 1974, pp 88, 100.
63. Dr Koch's discovery, *NY Tribune* August 26, 1894, p 6.
64. The new foe of diphtheria, *NY Times* September 6, 1894, p 4.
65. The foe of diphtheria, *NY Times* September 20, 1894, p 4.
66. Antitoxine for the poor, *NY Herald* December 10, 1894, p 3.
67. The new antitoxine, *NY Herald* December 10, 1894, p 3.
68. All eager for antitoxine, *NY Herald* December 11, 1894, p 3.
69. Antitoxine to save life, *NY Herald* December 17, 1894, p 4.
70. Antitoxine is greatly needed, *NY Herald* December 12, 1894, p 3.

Molecules and magnets

LOIS GREENE STONE

It was the 13th day of the month. I was born on a Friday the 13th, and I was not going to allow a date, or superstition upset me; the sight of the procedure room did that.

I had already been asked about my previous operations to determine if any metal objects resided in some internal body fold. My credit cards, with their magnetic strips, were secreted away in a metal file box along with my clothing. With no bra, and wearing only a long-sleeved turtle neck shirt, pastel pink nylon underpants (after I had removed my corduroy slacks), and socks, I was more ready for bed than for a medical procedure. I wore a short-sleeved gown like a bathrobe over my shirt and panties, and all I needed was a toothbrush and rinsing cup to convince myself that I was at home.

A long table, stretcher-sized in width, projected from a circular metal tube. I knew I would be inserted into the tube and would remain there for almost 45 minutes; I tried not to panic.

This was not the magnet of childhood games—the horseshoe-shaped piece of metal that I stuck into places to annoy my mother, or used to suck up all her hairpins so she had to pull each away to pin her snood in place. I didn't know about polarization, dipoles, atoms, or fields, only how to grab paper clips, the springs on new clothes pins, garters, and sanitary napkin belt clips.

I lay on the table, glad that I was skinny enough to fit. Did heavy people fear being stuck in the hole? Did anyone ever ask? My arms were strapped down, and I thought of the movie *One Flew Over the Cuckoo's Nest* and lobotomies. Don't think yet, I told myself. I was covered with a blanket and then the table was pushed deep into the tunnel. I heard the heavy entry door being sealed shut. No one had prepared me for this or for any other part of the medical test. Why not? The booklet in the nuclear magnetic resonance imaging waiting room had cartoon characters displaying what goes on during the procedure. A large smile was on the sketch's face, while he or she was inside the machine. I could not imagine anyone smiling. I felt that the booklet showed no respect for real emotions and made no allowances for people to express anxiety. Just pretend there is no anxiety . . . fragmented thoughts . . . my nose itched.

A voice on a microphone told me I would hear clanking; this first test would take six minutes. Six minutes. No clocks. Twenty-six, staccato, clanks echoed in my small space. Then I had six minutes of grinding sounds: Mississippi-one, Mississippi-two, Mississippi-three. I tried to minimize my terror. I had written an article for *The San Francisco*

Chronicle on the dangers of electromagnetism in household electric blankets. Yet, I lay there being bombarded with electromagnetic waves. It is safe? When I had cranial radiation during the 1940s, I was told that it was safe, bloodless, and would definitely replace the surgeon's knife. My young body was placed in a lead-lined room, and I was alone with sandbags holding me in place. Years later, scientists screamed danger. Well, when years later come for this procedure, I will be too old to be concerned for the future. I tried to find humor.

Were my arms trembling because of the radio waves being introduced into my magnetic iron lung and the resonating of my body's atoms. This machine certainly looked like an iron lung. Today's young people might not realize this as they have probably never seen an iron lung. I had no mirror to see anything and, with my head secured, my eyes could only see that I was trapped in a small beige space. Thank goodness no one decided to paint the sphere red. Again, humor. At least I had momentarily distracted myself enough to forget my itchy nose, until the urge to touch it returned.

A voice. The next test would last 12 minutes. How would I get through it. I did not even ride my stationary bicycle that long. What will the computer show the radiologist when he looks at the signals from the nuclei of my atoms? Will whatever it is be fixable? Why doesn't anyone care what I am thinking or feeling? A procedure without the need to cut, sew, or inject dye does not make it any easier to endure. With a surgeon, you are either asleep or numb. I was awake and feeling helpless. I sensed a quiet terror, thinking that everyone would depart the office, that I would be left in this cylinder unable to remove my straps, and that I would suffocate. During the last week of my pregnancy, I was certain that I would carry the fetus forever, regardless of nature's time clock. The same kind of irrational thoughts were now taking place. The grinding stopped.

Is anyone coming? Is it over? I multiplied the minutes and knew the answer. Don't flinch. Lois, I commanded, else the entire test will have to be repeated. I ordered my quivering knees and arms to cease their automatic contractions.

When the test was over and I was wheeled from the small hole, I was expected to respond "I'm okay" when the technician asked, "Are you okay?" I wasn't okay. I needed to hear someone's voice reassure me that the end would be soon, and then give me a verbal gold star of encouragement.

Because of my polite upbringing, I simply said "thank you," feigned steadiness as I redressed, carefully walked to my car, and, in its privacy, cried.

Address correspondence to Ms Stone, 5 Wide Waters Lane, Pittsford, NY 14534.

Psychic advisor

NAOMI BLUESTONE, MD

Doctor: "\$50.00 for a house call?! Why, even I don't get \$50.00 for a house call!"

Plumber: "Neither did I when I was a doctor!" (Old Joke)

Having finally attained a level of professional insult with which I will not put up, I have resolved upon a most unusual course of action. I present it to readers of the *Journal* to consider as a possible alternative for the future. My idea started as no more than a whimsical fancy engendered by terminal desperation, nor did I ever intend it to become the sort of proposal to which a reasonable soul would give much credence. However, it would not go away; I found myself ruminating night and day on the feasibility of turning a satirical and infamous notion into the final reality of my professional career. Soon, I had determined on closing my office for the private practice of psychiatry, relinquishing my license to practice medicine and surgery (with all the perquisites and benefits pertaining thereto), and resigning from all those professional associations which had supported me in my career goals for the past 30 years. I decided to efface the persona of Naomi Bluestone, MD, MPH, once professor and commissioner, now rural practitioner of general psychiatry, and become Blessed Naomi, the All-Knowing, Psychic Advisor to the Sick at Heart, and Reader of the Great Unknown. As a renegade and outlaw practitioner, liberated once and for all from the corporate madness engulfing the physician, I would be free to fulfill the Hippocratic oath I made the day I was granted my diploma in *ars medicus*.

The heady idea of being free at last, free at last (and so forth) from the yoke of what was once a noble profession made me hee-haw like a happy donkey and kick up my rear legs in glee. What follows is the rationale for this decision, and the blueprint that I have established for its successful fruition. Although the details remain to be implemented, the philosophy underlying my unique transmutation should not be unfamiliar. It is predicated on the belief that if the guardians of the bottom line (GBL) will not permit me to practice medicine the way I was trained, which I, fool that I am, still believe is the only morally correct way, than I am justified in giving up the title physician and adopting any appellation which will enable me to practice my calling without impediment. If I can achieve good results as a fringe element, an unlicensed and unregulated psychic advisor, accountable to no one and nothing save my own superego, so I shall become. As the poet would say, "A role by any other name would smell as sweet."

For those who consider a move from physician to psychic healer as retrograde, please consider that there is an historic precedent in going underground. Five hundred

years ago, when Torquemada ruled Spain at the behest of his Catholic sovereigns, my forebears became conversos who continued to practice their faith in the basements of their homes. Were they not still Jews in the eyes of the Almighty? When the reign of terror by the gastropods was over, did not many of their descendants return to the faith of their ancestors? My Machiavellian ruse is dedicated to their memory.

If you remain unconvinced, consider the historical footnote often quoted by Dr Lowell E. Bellin, former Commissioner of Health of the City of New York. He grimly cited the doomsday activities of the European monasteries, whose monks kept books, civilization, and culture alive in their dank castles, while all around them burned the Dark Ages. Won't this country need undercover agents like me to surface once again when the short-sighted affair with the Age of Technocracy starts to come apart?

It should not be necessary to belabor the provocation for my adoption of another *modus vivendi*, but permit me to vent for a few moments. There are times when the practice of medicine seems like a quicksand of lost assumptions, a moral quagmire sucking and burying our very marrow. Like peat bog soldiers, we carry our spades to the bog each day and dream of homeland, for our reality is onerous. Countless empty hours have been spent complying with the unholy mess created by the demands of the GBL and their shock troops, the alphabet soup police (ASP). The paperwork's up. The income's down. The censures are up. The satisfactions are down. The harassment is up. The productivity is down. (Someone could write a song about it.)

The necessity for additional help to process the minutiae has escalated office costs and cut income significantly, particularly for the non-sub-surgical specialists who have proven so singularly unadept at manipulating an increasingly decadent system to their advantage, they now find themselves struggling to provide their families with what were once essentials: college tuition, summer camp, and electronic toys, such as periodic updates on software. The time it takes to learn how to beat the system, play the game, cultivate the code words, and automate the boilerplate could as well be spent acquiring another doctorate.

Worst of all, a development that I have found ethically intolerable and therefore emotionally insufferable is that the GBL and ASP are now interfering directly, stupidly, and quite maliciously with the promise I made to my patients on that rainy day in June 30 years ago at the Academy of Music in Philadelphia. They intrude themselves like busybody in-laws into my decision making, they trample on my clinical judgment, and they employ scabs at high salaries who, get this, still demand and get collegial respect.

Address correspondence to Dr Bluestone, RFD 1, Box 517, Center Barnstead, NH 03225-9720.

How hard it has been on those of us living through this interim era of American medicine, what the Chinese would undoubtedly call "interesting times!" The prolonged interregnum between the open frontier and a state-regulated industry has turned to chaos what was once the primary pursuit of medicine: treating patients equitably, educating the students, and always searching for the better medical mousetrap. Only human need seems to remain, and more grievous than ever. The pain of the race horse chained to a milk wagon is the fate of today's aging physician. It is all so familiar to readers of the *Journal* that merely recounting the agony constitutes a vinaigrette soak on an open wound. As another old song goes, it's been said, so many times, so many ways. . . .

Blessed Naomi sees no hope of reversing the tide of degradation. Upholding basic principle is consistently misinterpreted as a venal desire to preserve an elitist life style. All appeals to senior colleagues to be brave, to fight, to institute civil disobedience have been doomed to ridicule. I must sound like the aging elite of the AMA, or my colleagues in Orange County of a generation ago, with whom I never could agree. Whenever I lift up my voice in song, I am simply told that if I don't cooperate with the forces of progress, the decisions will be made for me. My choice, not unlike Sophie's, is stark: to be co-opted, or to be run over and effaced from off the surface of the earth. Whoever thought the day would come when a reasonably responsible practitioner would have to choose between leaving medicine or sleeping at night?

So I figure by becoming a fringe practitioner, what's to lose?! You don't need to be a weatherman to feel the north wind blow, and you don't have to consult a union official to know which side you're on. (Oh, Bernstein, Dylan, and Guthrie, where would we be without you?)

It's time for me to get out, but where else to go? Reality raises its ugly head at every turn. A former career in a poorly paid specialty and now a rural practice in a time of general impoverishment leave this squarely, middle-aged woman with insufficient funds to declare a pox on all the houses of the enemy. The law of the jungle dictates that the tax-deferred savings remain untouched for another 42 months (but who's counting). Like every other member of the class of '62 who'd like to get out before the ulcer perforates, I'm too old to retrain in another career and too young to quit. Besides, I had always promised myself that having given up my youth and all its perks steeped in the 24-hour study of medicine, I would practice until I was a justly revered old lady with sensible flat shoes and long white hair pinned up in a bun. It is hard to repudiate the beliefs of a lifetime. No, no, better that I should reincarnate as Blessed Naomi, the wise old crone, plying her trade beyond the reaches of managed care. But now, you ask incredulously, how will I pull this off? Trust me. It will be done in such a yeomanlike manner, the ASPs will never be able to lay a letter of condemnation on me. Herewith my game plan.

First of all, I'll need a counsel chamber. There will be no need to renovate my present office, which mercifully is already on the second floor. I will have a fisted hand painted on a wooden sign to hang outside the door, with the thumb and index finger pointed upward. (I have been tempted to change the number and direction of the pointing finger to reflect more accurately my mood, but bow to good taste.) My office furniture will remain unchanged, the oriental carpets providing a faint aura of the mystical

east. A full wall of bookshelves will remain for my personal use but will be covered with a curtain; this area will remain permanently shrouded in the mystery requisite for my new career. My diplomas will be removed from the walls, intimidating evidence that I have come from the world of the educated and unfeeling. They will be replaced with misty prints of little girls with huge dark eyes, patting luminescent lambs and incandescent puppies. The waiting room library will be replaced with ceramic chatchkies, sleeping Dalmatians, pink ballerinas, a snowman with a red scarf. I will install a coffee machine and a daily supply of doughnuts; a tasteful but inexpensive cosmetic or jewelry concession may even be permitted. This should complete the ambiance for the sea change of a psychiatrist into a psychic counselor.

My appearance, too, will be modified, a corporeal relief and a financial boon. Unloading tailored outfits, nylon hose, high-heeled pumps, and discreet jewelry on the local re-sale shops, I will affect comfortable and flowing garments of a silky and colorful fabric, the better to cover my middle-aged spread. I will wear satin mules, although I may have to dig them up specifically for the purpose and scuff them around a bit. The silver curls outlining my still youthful face, will enhance my image as a knowledgeable source of comfort. My male colleagues could never pull this off, being of an utterly useless sex for this purpose, nor could the callow young women who would clearly fail to inspire confidence in those who need representatives of Mother Earth to heal their troubled hearts and psychological complaints. ¹⁴

Personally and professionally outfitted, I will now be ready to open my doors. I have given thought to the best way to build a following from those who are easily intimidated by doctors because I do not underestimate what a challenge it will be. I anticipate difficulties, for example, reconciling my vocabulary with those of simple women, who feel more comfortable with chiropractors, palm readers, and manicurists.

Rest assured that unlike the utilization reviewers of the GBL, who do not hesitate to let their grasp exceed their expertise, I will not set up shop until I am in command of what I am doing. I intend to take a PR course of the kind given to those who manage for-profit psychiatric hospitals, the better to polish up my glib. Then, I will observe and copycat a few alternative practitioners, probably under cover, to determine what makes them successful. I may even apprentice myself to Gifted Mary or Awesome Nora to ensure that my credibility with my new case load will be airtight. Content will not go unreviewed: I'll brush up on how to lure a straying husband back and still retain a functioning immune system; how to keep a kid off dope without chaining him to a post in the cellar; how to know if the dark stranger is Mr Right, or just another sleaze coming out of his third marriage and his shirt buttons. However, I have no doubt that the skills I already possess will make me an overnight success.

As with any new career, getting started and building a customer base is the hardest part. I see nothing wrong with a knock 'em dead advertising campaign in the local newspapers, and half-page ads in the Yellow Pages such as those used by the plastic surgeons. My announcement will not betray my origins or my still-practicing colleagues; I believe it gross and tacky to exploit the "Try Getting That From a Doctor!" theme. It would simply state: Blessed Naomi is available to give counsel and guidance on all affairs of the

heart, body, and soul, and brings to her gift many years of experience. No one has to know that this has included 15 years of higher education, delivering almost 100 babies, surviving two residencies, functioning within any number of bureaucracies, and finally dropping out of one of the most prestigious careers this country once had to offer. What they don't know won't hurt them. Word of mouth will probably be my best referral source, and provide an invisible barrier against intrusion from the ASP. (Needless to say, I will burn all 600 remaindered copies of my book, *So You Want To Be A Doctor: The Realities of Pursuing Medicine as a Career* [1981, Lothrop, Lee & Shepard, New York,]).

Everyone needs a shtick, even ethical practitioners of medicine, but there should be no need for me to have to learn astrology, Tarot cards, ball gazing, advanced Roling, or anything like that at my age. Having mastered multiple personality disorder, post-traumatic stress syndrome, and other iffy/trendy diagnoses, I should probably find these activities a piece of cake, but no, I will not play that game any more. I have decided that my claim to a quarter hour of fame will be based on my capacity to draw from the patient herself the very answers to the questions she seeks! It's probably somewhat of a novelty in the advisor trade, but it could work. Instead of telling the client authoritatively what no other person can ever really know, I will so engage her in the process of self-discovery she will be as satisfied with my wisdom as my psychotherapy patients are now. Leave it to me. In my former life, this process would have been a routine intake interview with appropriate follow-up and psychotherapy, but now it will be called a series of life readings. The end result will be the same.

By now, you have some sense of how my training in psychotherapy will be used in an unsophisticated population. It is unfortunately true that it closely resembles what we now know as short-term dynamic psychotherapy, but since the managed careniks don't permit legitimate practitioners to do anything else nowadays, no harm will be done that has not already been done. It is also true that this is hardly the population that we might have selected to provide ideal psychotherapy candidates, but then it has been a long time since we have seen anyone with the capacity for significant, long-term, introspective work.

To accommodate those for whom readings are insufficient, and who require some tangible object to enable them to borrow strength when life gives them the kind of beating that the medical profession has endured, I have set in a store of amulets, good luck charms, and rabbit appendages for purchase at a nominal price. After years in psychiatric practice, I am familiar with the most commonly used "transitional objects," and see no reason why they should not be purchased directly from me. For bona fide seasonal depressives, I will purchase broad spectrum lights, and probably charge a modest fee for the use of them by the half-hour. The anxiety disorders will do time in my cocoon chair, with relaxation tapes, song birds, and The Four Seasons. The price will be right.

But, you say, what about the question of psychotropic medication? Can that really be ignored? Of course not! May I point out that my new clientele rarely has access to medication right now, by virtue of ignorance, prejudice, poverty, and the corporate greed of the ethical drug companies. I shall have to devise a way to bring it to them, now that I myself can no longer legally write script. I plan to introduce these and other somatic treatments from my safe niche beyond the pale, my secure spot in that untouchable never-never land of the occult healer.

I want you to appreciate how truly clever I am. I intend to set up a long table covered with Damask cloth, lined with ruby glass bowls. Each of these will contain a well-disguised, over-the-counter medication. I will keep a generic aspirin for pain, an anti-histamine for sleep, a psychostimulant for fatigue, a natural desiccant for pre-menstrual tension, and so forth. There will be a few vials of cool liquid, white wine, grape juice, and the like for other common complaints. All will be endowed with whatever placebo purpose I wish to ascribe to them. I will go hog wild inventing aphrodisiacs, all of which will work quite well, and the manufacture of which might constitute a side-line black ink business. None will require a medical prescription, so the BNDD will have no reason to look over my shoulder as I dispense these according to my best judgment.

If all else fails, and I truly believe that a customer requires a traditional psychoactive drug, I have devised a method whereby it will be obtained. I plan to keep a stable of competent physician acquaintances with whom I will work closely. As each customer leaves, I will hand her a sealed envelope with personalized instructions. I will instruct the customer to hand deliver it only to the physician I highly recommend, and to insist that it be burned in her presence lest the efficacy be diminished. Each envelope will contain a message. One might say, for example, "This one requires a tricyclic. And none of that 10 mg at bedtime garbage. Get her up to 150 as fast as you can and then monitor her bloodwork. Call me for questions. Did you get that reprint on alternative professions that I sent you last week?"

Another might say, "This woman says her relatives are accusing her of paranoid ideation, but I notice that she is quite deaf. Please check her out and then tell her to come back to me in a month. Thanks a lot. See you at the Bader's on Saturday night."

A third would say, "I used to treat this girl's mother when I was a psychiatrist. Medication receptivity often runs in the family. Try haloperidol with an anti-Parkinsonian agent of your choice, and she'll probably stop hearing the voices right away. If not, see if you can get a bed for her on 5-W."

All in all, I think it would work. There should be no difficulty in establishing an ethical, confidential arrangement with cooperating physicians, all of whom, I presume, would be in my position but for the fact that they happen to be a bit younger and still have kids to get through college. There would be no temptation to split fees, as I will be enjoying my first "volume" practice in 30 years, and I never did that when I was a doctor, so why should I start doing it now?

By the way, I have not yet discussed my proposed fees. I figure that I can afford to cut them by over half and still make the same net income. Just figure out for yourself how much I can save by not needing a staff, an office, a phone or a fax. (We alternatives do walk-ins only.) Think of the time saved by not having to make appointments, or report my nefarious activities to the itchy-bitsy bureaucracies. Imagine not having to fill out one single form! Not having to maintain a malpractice insurance carrier in the style to which he is accustomed! Not even having to keep a clinical record unless I wish to! In addition, consider the burst of creative energy I shall experience knowing that I am loved, respected, valued once again! Yes, I can well afford to discount my services.

I also believe I will have no dearth of paying customers. My clientele are reconciled to spending dearly for their beauty salons, cosmetics, exercise machines, and psychic

readings. Remember what this population spends on lottery tickets, those little luxuries that enable them to endure life with their meal tickets? When they are in pain, they will see me as their friend, not as the unwelcome aftermath of a malignant fate. I anticipate an all cash business, for women tend to be forced to raid household money for their personal needs, having no other source of income. And tragically enough, many do not even know how to use a checkbook. (Actually, I will derive satisfaction from teaching them street smarts without feeling that I am transgressing therapeutic boundaries.) Fear not, colleagues, I shall prosper. Although I am too old a dog to cart all that money to the bank in a wheel barrow without informing the IRS, I will certainly enjoy unloading each deposit.

Please understand that not all the bugs are out of my scheme yet. I still haven't figured out what to do with clients who may need to be admitted to an in-patient unit. I will miss Grand Rounds, even if the information was canned, the speakers dull, the gossip unnecessary, and the financial base of the pizza luncheon ethically questionable. Worst of all, my thought provoking essays will now be considered unpublishable, except by the weirdest of throwaway editors. In addition, I know it will be lonely. Shunned by the body medico-politic, and finding my dinner invitations turned down cold, I may even have to form friendships with my clients, verboten when I was psychiatrist. However, I will survive, in spite of accusations of being a fanatic, a pervert, a turncoat, and a hideous example of what the climacteric can still do to women.

It has been pointed out to me by advance readers of this essay that I have no assurance that regulation by the state may not be brought to my new career as an alternative practitioner, but I see little likelihood of that. Most states have a long history of letting charlatans practice undisturbed. It will take the authorities a goodly amount of time to make sure that all the social workers, psychologists, and other personnel who have steadily chipped away at the psychiatrist's function will be brought under regulation. In addition, when that is accomplished, the fight over prescribing privileges for psychologists should take up a few more years. Next to fall will be the pretensions of those with

legitimate degrees in other subjects, transferred to my area of expertise by a stroke of wishful thinking. By the time they get to psychic advisors like me, I shall have folded my tents like the Arabs. "Advisors" can slip through the net and re-establish themselves down the block as "readers;" "readers" can as easily become "celestial counselors." Never forget that we quacks and feel-goods are more fluid than you doctors. In fact, now you all know what it feels like to be treated the way we were in the last century!

Perhaps I am premature, but if I make a go of my new venture, I am thinking of starting a support group for former colleagues who have been carted off to Valhalla before their mortgages are paid off. (We might call it The Ex-Psychiatrist Society, or something equally cute, and give it a catchy acronym like EPS.) We members, united by our beliefs in transcendent values rather than specific advocacy for certain medico-political systems, could help ourselves recapture the ego strengths we had before we became expendable providers. We could share early memories of those who lived in the days of giants, when medicine had hair on its chest and the soft, cool hands of an angel. Once productive individuals could kaffee klatsch about what careers they have drifted into now, and how they incorporate the insights gained from those long-lost days when they used to be doctors. A flag should be designed and flown on Sir William Osler's birthday, at an annual pilgrimage made to his grave to keep him from turning over. (That would be, as the next generation is wont to say, a real fun thing to do.) Insightful position papers could be issued with the theme of re-inventing medicine, although, sadly, these will inevitably be considered futile assaults on the ruthless by the toothless. It might even be possible for old dogs who don't want to turn tricks to band together and provide some service to the country, never mind the fires of health care conquest still burning around us.

However, now I must get on with my work. If there is any one who feels strongly that my proposed course of action is inappropriate, criminal, hurtful, or unethical, please speak now or forever hold your peace. I am preparing my letters of withdrawal at this very moment, and I will soon be shopping for a nice pair of mules.

Mediastinal teratoma presenting as empyema

HERBERT H. SCHERZER, MD; KAUSHIK J. PATEL, MD; JOHN J. VOTTO, DO; LOUIS BROWN, MD

Benign teratomas are germ cell tumors that consist of mature tissues derived from ectoderm, mesoderm, and endoderm. They account for 3%–12% of mediastinal tumors. Most (50%–60%) are asymptomatic and are discovered on routine chest radiographs.¹ Dyspnea and substernal chest pain are the most common symptoms. Rarely, teratomas may rupture into the pleural space-inducing severe serositis and effusion.^{2,3} Previously reported cases of ruptured teratomas have been characterized by a readily identifiable mass that facilitated the diagnosis. We present a case of a benign teratoma, presenting as an empyema, where the tumor appeared to represent a loculation and was not suspected until thoracotomy.

CASE REPORT

A 17-year-old girl presented with complaints of severe right chest pain and fever. Two weeks before admission she was seen by her pediatrician for indigestion and was given a prescription for ranitidine. Her condition improved over the following week. After moderately vigorous aerobic exercise, lifting one pound soup cans, she experienced right-sided chest pain exacerbated by right arm movement and by deep inspiration or cough. She was seen the next day by her pediatrician, who prescribed acetaminophen with Codeine for a muscle strain. The pain persisted, and a fever developed. The next day she was seen in the emergency room and a chest radiograph demonstrated a right pleural effusion.

Her past medical history was unremarkable except for tonsillectomy at age of 16. She did not smoke. Her medications included ranitidine, 150 mg twice a day, and acetaminophen with Codeine as needed. She was allergic to penicillin. She denied using alcohol or illicit drugs. On physical examination, her pulse was 120 beats/min, respiratory rate was 44/min, blood pressure was 100/60 mm Hg, and temperature was 101.4° F. There was dullness on percussion and reduced breath sounds over the right lower half of the chest. The patient moved the right arm with reluctance because of right-sided chest wall discomfort.

The laboratory data were remarkable for a total white blood cell count of 20,100/mm³. The differential count showed 81% neutro-

phils, 5% bands forms, 4% lymphocytes, and 10% monocytes. The electrolyte levels were within normal limits. Serum protein was 5.8 g/L, and serum lactate dehydrogenase (LDH) was 178 IU/L. Arterial blood gas findings on room air were the following: pH 7.42; PaCO₂, 35 mm Hg; PaO₂, 76 mm Hg, SaO₂, 92.1%. Chest radiograph (Fig 1) showed elevation of the right hemidiaphragm with opacification of the lower half of the right lung; decubitus views showed layering of fluid. A thoracentesis of the right chest yielded turbid pinkish-brown fluid. Analysis of the fluid showed a glucose level of 74 mg/dL; protein of 5.03 g/L; LDH of 526 IU/L; pH of 6.18; white blood cell count of 78,000/mm³; red blood cell count of 9,700/mm³; differential count of 80% neutrophils and 20% monocytes. A gram's stain of the pleural fluid showed numerous neutrophils and debris, and a smear for acid fast bacilli was negative. The fluid was re-inspected and no organisms, hairs, squamous cells, or keratinous material was seen.

The patient was thought to have an empyema. As no organisms were seen on Gram's stain, she was started on intravenous erythromycin, 500 mg every six hours and clindamycin, 600 mg every six hours for 14 days, to cover for possible atypical and anaerobic infections. A chest tube was inserted into the right chest which drained 1,000 mL. An additional 650 mL drained over the next three days.

Sputum culture showed oral flora and a pleural fluid bacterial culture was negative. Viral and Legionella titers were negative. The patient continued to have a low-grade fever up to 100.7° F. A repeat chest film showed a persistent opacity at the right base. A computed tomography (CT) scan showed a large, relatively homogenous density (6.5 × 7.8 cm) anteriorly up to the level of the carina, with

air bronchograms posteriorly (Fig 2). The Hounsfield units of this mass ranged from 4 to 12, consistent with a fluid-based density. This density was thought to represent either a loculated empyema or atelectatic lung. A repeat chest film the next day showed improvement in the right basal opacity, and therefore conservative management was continued. However, over the next few days the patient continued to have a low-grade fever up to 101° F. A repeat CT scan did not show any significant change. A second chest tube was placed anteriorly, which drained 110 mL over the next 24 hours. A follow-up chest film showed significant change, and the fever persisted.

The patient was taken to the operating room for thoracotomy to establish open drainage. Intra-operative fiberoptic bronchoscopy was normal. On opening the right chest, a solid mass was palpable. An ovoid mass (9 × 9 × 4 cm) was excised from the right mediastinum. The cut surface of the mass demonstrated multiple cysts containing friable, cheesy material with a zone of hemorrhage (rupture site) within the cyst wall. Microscopic study revealed mature tissues representative of all three germ cell layers, including pilosebaceous units, apocrine and exocrine glands, salivary glands, gut epithelium, pancreatic tissue replete with islets of Langerhans, choroid plexus, bronchial cartilage, and fat (Fig 3). No malignant changes were seen. This was consistent with a diagnosis of benign cystic teratoma. There were areas of ulceration and hemorrhage within the cyst and inflammatory changes in the surrounding pleura and parenchyma; all cultures at the time of surgery were negative. The post-operative patient's recovery was uneventful.

One-year after the resection, the patient is asymptomatic without any clinical or radiographic evidence of pleural inflammation.

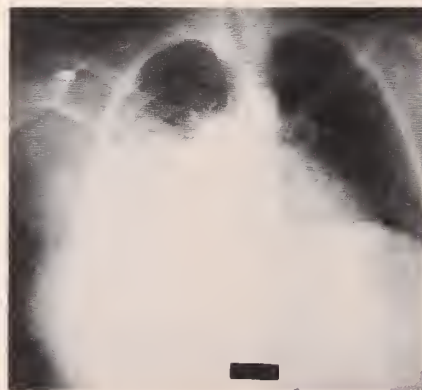


FIGURE 1. Chest film demonstrating opacification of right lower hemithorax by effusion.

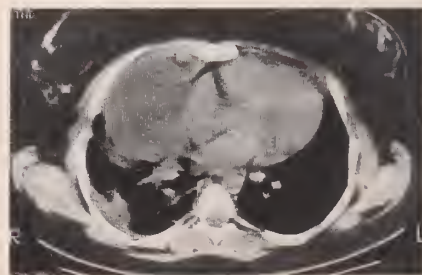


FIGURE 2. CT scan showing right-sided opacity consistent with loculated empyema.

From the Department of Pulmonary Medicine, New Britain Memorial Hospital, and the University of Connecticut, New Britain, CT.

Address correspondence to Dr Scherzer, Medical Pulmonary Director, New Britain General Hospital, PO Box 100, New Britain, CT 06050.

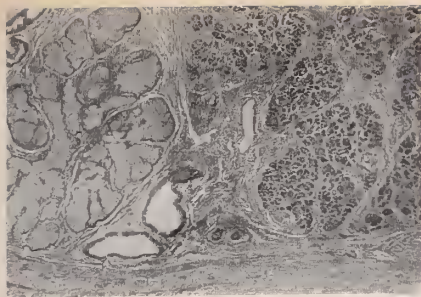


FIGURE 3. Photomicrograph demonstrating skin appendages and glandular tissue (hematoxylin and eosin stain, original magnification $\times 200$).

DISCUSSION

The majority of mediastinal teratomas are asymptomatic at presentation. When symptoms occur, typically the patient experiences retrosternal chest pain and/or shortness of breath. Rupture of the teratoma into the pleural space causing severe serositis is extremely rare.²⁻⁴ In 1944, Rusby⁴ hypothesized that before the advent of chest radiographs, a dermoid cyst presenting as an apparent empyema could only be diagnosed at thoracotomy. With present radiologic techniques, most teratomas can

be diagnosed before surgery, when a mass lesion with associated calcification (teeth or bone formation) is seen on chest film.

It might be expected that a chest CT scan would accurately differentiate a teratoma from a loculated effusion on the basis of Hounsfield numbers, given the different densities of fluid, fat, and calcium. CT features of ovarian teratomas are sufficiently pathognomonic to permit correct diagnosis in about two thirds of cases. Calcium and fat densities can be identified with a high degree of certainty by CT scan, helping to make the diagnosis of teratoma. However, proteinaceous fluid, hair, and other debris have non-specific characteristics on CT scan.⁵ The lack of calcification or of significant fat content accounts for the failure to diagnose the teratoma in this patient before surgery. Cobb et al² have suggested that the presence of squamous or columnar epithelial cells, enucleated squamous cells, hairs, calcospherites, keratinous material, and cholesterol on cytologic examination of thoracentesis fluid should strongly suggest the possibility of a ruptured benign cystic teratoma. These features were not present on the initial Gram's stain smear of the pleural fluid of this patient.

Hanten et al³ have postulated that high intracystic pressure from accumulated fluid or necrosis of the cyst wall caused by impaired blood supply would lead to rupture. Cobb et al¹ reported trauma as a cause of teratoma rupture. The cause of the rupture of the teratoma is uncertain in this patient. This case demonstrates that, occasionally, an inflammatory exudate may mask a noninfectious intrathoracic process such as a teratoma, and that CT scan cannot always be relied on to exclude the presence of a complex cystic mass, such as teratoma, in the mediastinum.

REFERENCES

1. Cobb CJ, Wynn J, Cobb SR, et al: Cytologic findings in an effusion caused by rupture of a benign cystic teratoma of the mediastinum into a serous cavity. *Acta Cytol* 1985; 29:1115-1120.
2. Hainsworth JD, Greco A: Mediastinal germ cell neoplasms, in Roth, Ruckdeschel, Weisenberger (eds): *Thoracic Oncology*. Philadelphia, WB Saunders, 1989, pp 478-479.
3. Hanten SJ, Keyes TF, Meyer RR: Spontaneous rupture of mediastinal dermoid cyst into the pleural cavity. *Radiology* 1955; 64:348-351.
4. Rusby NL: Dermoid cysts and teratoma of the mediastinum. *J Thorac Surg* 1944; 13:204.
5. Thoeni RF: Computed tomography of the pelvis, in Moss AA, Gamsu G, Gennant HK (eds): *Computed Tomography of the Body*. Philadelphia, WB Saunders, 1983, pp 1016.

Missed diagnosis of acute arthritic gout in kidney transplant recipients

INDRA D. DANIELS, MD, ELI A. FRIEDMAN, MD

Hyperuricemia and clinical gout may complicate the course of renal transplant recipients.¹⁻⁴ The occurrence of an acute attack of gout in an otherwise stable transplant patient may lead to a misdiagnosis of osteoarthritis or joint sepsis delaying effective treatment for days to weeks. We report three instances of delayed (missed) diagnoses of monarticular gout in renal transplant recipients seen during one year on a service that performs approximately 100 renal transplants annually.

Case 1. A 45-year-old black woman, who developed renal failure because of hypertensive nephropathy, had a functioning renal transplant for five years before being admitted to the orthopedic service for surgical excision of a "septic" mass on her left index finger that had been enlarging for three months. The patient had no earlier history of gout or arthritis. The 4 $\times$ 4-cm mass, initially painful, was now nontender. She had been

seen on multiple visits to the transplant clinic where cultures of the joint aspirate had been negative. Polarizing microscopy of joint aspirate had not been performed.

The patient's post-transplant course had been complicated by new onset non-insulin-dependent diabetes mellitus, bilateral cataracts, *Pneumocystis carinii* pneumonia, and mild hydronephrosis of the renal allograft. Her medications included daily doses of azathioprine 50 mg, cyclosporine 200 mg, chlorpropamide 500 mg, ferrous sulfate 300 mg, furosemide 160 mg, clonidine 0.4 mg, and prednisone 7.5 mg. The patient was afebrile, and the white blood count was normal.

There was a mass overlying the proximal interphalangeal joint of the right index finger (Fig 1) measuring 5 $\times$ 4 cm. The finger was nontender, hyperpigmented, and freely movable; sensation in the finger was intact. Pertinent laboratory findings included a serum creatinine concentration of 2.3 mg/dL, a blood urea nitrogen level of 58 mg/dL and a serum uric acid concentration of 15.7 mg/dL. On the day following admission, the affected joint was aspirated, and the joint fluid examined microscopically under polarized light showed characteristic negatively birefringent needle crystals of uric acid. Treatment with allopurinol was begun, and the patient was dis-

charged without surgical intervention. Because of potential interaction between azathioprine and allopurinol, the dose of allopurinol was adjusted to 200 mg daily according to the guidelines published by Hande et al.⁵ Within two months, the joint



FIGURE 1. Radiograph of swollen proximal interphalangeal joint of right index finger in Case 1. There is a fracture of the metacarpal epiphysis suggesting that the finger had been subjected to unreported trauma as well as gout.

From the Department of Medicine, State University of New York, Health Science Center at Brooklyn, Brooklyn, NY.

Address correspondence to Dr Eli A. Friedman, Department of Medicine, State University of New York, Health Science Center at Brooklyn, 450 Clarkson Avenue, Brooklyn, New York 11203.



FIGURE 2. (Right, 1988) Extensive bone erosion characteristic of gout in both bones of the right first metatarsal phalangeal joint. There is soft tissue swelling of the great toe. (Left, 1987) Radiograph of the same foot taken one year earlier for evaluation of diabetic neuropathy shows no evidence of gouty arthropathy.

mass disappeared, and the serum uric acid concentration became normal.

Case 2. A 42-year-old white man, who had insulin-dependent diabetes mellitus since the age of 11, developed uremia at the age of 35 due to diabetic nephropathy. He had a single attack of gout of the right ankle ten years before the present complaint. After three years of dialytic therapy, a cadaveric kidney was transplanted without complication. Four years later, during a time of renal graft stability, swelling and erythema of the right great toe was noted and diagnosed as cellulitis by a podiatrist and a consulting surgeon (Fig 2). When seen in renal clinic, examination of the left foot disclosed erythema, warmth, and tenderness of the left first metatarsophalangeal joint. The patient was afebrile, and the white blood count was normal. Key laboratory findings included a serum creatinine of 3.5 mg/dL, a blood urea nitrogen concentration of 45 mg/dL, and a serum uric acid level of 6.8 mg/dL. Daily medications administered at the time of onset of arthritis were the following: cyclosporine 125 mg, prednisone 10 mg, furosemide 80 mg, clonidine 1 mg, prazosin 2 mg, and NPH and regular insulin according to finger-stick glucose levels measured four times daily.

Cephalexin, ampicillin, and erythromycin were administered for suspected osteomyelitis of the toe for six weeks during which time the pain and immobilization gradually im-



FIGURE 3. Radiography of left ankle in Case 3 shows neither soft tissue swelling nor typical bone changes of gout.

proved. A consulting rheumatologist, however, doubted the diagnosis of osteomyelitis and suspected gout, which was confirmed by aspiration of fluid from the affected joint and demonstration of needle crystals of uric acid under polarized microscopy. Bilateral tophi were noted in the soft tissue of the elbows. Allopurinol and analgesics were prescribed and the toe rapidly improved within one month while cyclosporine and furosemide were continued. The uric acid level remained normal (<7.5 mg/dL).

Case 3. A 32-year-old Hispanic former narcotic drug dealer developed renal failure due to heroin nephropathy. Four years after receiving a cadaver donor kidney transplant and episodic noncompliance with his immunosuppressive regimen, the patient presented with pain in the left ankle joint and a fever of 101° F. The white blood count was elevated to $12,600/\text{mm}^3$. He had no earlier history of gout or arthritis. Renal function had been stable over the preceding six months (serum creatinine of 3.8 mg/dL, blood urea nitrogen 38 mg/dL). The serum uric acid level was 12.2 mg/dL. Daily medications included cyclosporine 200 mg, furosemide 80 mg, prednisone 20 mg, minoxidil 5 mg, and clonidine 0.3 mg. A diagnosis of septic arthritis was made and empiric treatment with cefazolin was begun without defervescence over five days. Multiple blood cultures failed to grow organisms. A rheumatology consultant suggested the diagnosis of gouty arthropathy but was unable to aspirate joint fluid on two occasions. Treatment with colchicine 0.65 mg/hr was started. The patient became pain-free, had a normal temperature within six hours, and was discharged on an outpatient regimen of allopurinol. The patient continued minimally compliant with his medication regimen. Six months later, the patient was hospitalized for fever of 100.9° F and acute left ankle pain that was thought to be acute gouty arthritis by a consulting rheumatologist; it responded within hours to colchicine treatment.

DISCUSSION

Hyperuricemia is a recognized metabolic consequence of cyclosporine therapy, occurring independent of nephrotoxicity in 30%–60% of patients, depending on how hyperuricemia is defined. Gouty arthritis is the major clinical manifestation of hyperuricemia and has been described in both renal and heart transplant recipients.⁶ There are reports suggesting that 4%–10% of all cyclosporine-treated patients develop gouty arthritis. The average time from kidney transplantation to the first attack of gout is about 24 months.

Hyperuricemia in this population appears to be a consequence of decreased urate clearance rather than a consequence of overproduction of urate. Many pharmacologic agents have been associated with hyperuricemia, and sometimes gout, not by interfering with renal tubular excretion of urate, but also by increasing formation of uric acid.⁷ Ethyl alcohol and diuretics are the most commonly implicated drugs, but salicylates, pyrazinamide, ethambutol, nicotinic acid, 2-ethylamino-1,3,4-thiadiazole,

fructose, and cytotoxic agents should all be suspect. Cyclosporine is more likely to cause hyperuricemia and gout than is azathioprine.³ Rapid lowering of serum uric acid concentration by allopurinol or uricosuric drugs has been reported to precipitate acute attacks of gout.

In a retrospective analysis of renal transplant recipients treated with either cyclosporine and prednisone ($n = 129$) or azathioprine and prednisone ($n = 168$), gout developed in nine patients in the cyclosporine group but not in any patients in the azathioprine group. Importantly, serum urate levels became elevated in 90% of patients treated with both cyclosporine and diuretics compared with 60% given cyclosporine without diuretics. Several factors probably contribute to this: cyclosporine-induced nephrotoxicity, use of diuretics, and possibly a direct effect of the drug on the tubular transport of urate. On the basis of a study of urate metabolism in six cyclosporine-treated patients, Lin et al inferred that the mechanism of hyperuricemia was a "decreased renal urate clearance."³ Gores et al also found a high incidence of hyperuricemia in cyclosporine-treated renal allograft recipients.⁸ Of 131 recipients treated with cyclosporine and prednisone, 80% manifested hyperuricemia (serum uric acid >8 mg/dL), and clinical gout developed in six. In contrast, hyperuricemia was noted in only 55% of the azathioprine- and prednisone-treated group, and none developed clinical gout. The initial presentation of gout post-transplant may be that of a destructive arthritis as detailed in Cases 1 and 2 above. Failure to recognize gout in these two recipients resulted in unnecessary hospitalization, exposure to toxic antibiotics, and prolongation of joint pain. In both cases, the diagnosis could have been made by the relatively simple outpatient procedure of joint aspiration with use of polarizing microscopy, as suggested by the history. Radiographs in these two patients were highly suggestive of gout. Fever and leukocytosis was present in only one of our three patients (Case 3). In Case 3, the patient's background of heroin abuse understandably directed thinking to a septic joint complication. Treatment with colchicine, started on the basis of a typical clinical picture of gouty arthropathy in the presence of hyperuricemia, induced prompt regression of inflammation.

In all three patients, the correct diagnosis of gouty arthropathy permitted specific therapy. When prescribing any medication for a renal transplant recipient, it must be kept in mind that after many "successful" transplants, recipients have severely reduced renal function as evidenced by creatinine clearances in the range of 25 to 60 mL/min.

Allopurinol, an inhibitor of the last stage of urate synthesis, reduces the risk of repeat gout attacks but may potentiate the leukopenic effect of azathioprine,⁹ a drug interaction requiring careful observation.

The dose of allopurinol should be reduced to 75% of that determined by use of the table constructed by Hande et al.⁵ when given concomitantly with azathioprine.¹⁰ As examples, a patient with a creatinine clearance of 10 mL/min should be given a maintenance dose of allopurinol of only 100 mg/day, whereas a dose of 200 mg/day is appropriate for a creatinine clearance of 60 mL/day.

Colchicine given orally is effective in improving the symptoms of an acute attack of gout. Approximately 10%–30% of colchicine is excreted in urine, the remainder in feces. Therefore, reduction in dosage of colchicine in renal insufficiency is not needed unless the creatinine clearance is <20 mL/min when the daily dosage is decreased to 50%. Prolonged administration of colchicine should be avoided in transplant recipients whose creatinine clearance is <50 mL/min. The acute treatment of a gouty attack can be managed by oral administration of colchicine 0.5 mg each hour or 1.0 mg every two hours until

the patient experiences relief, gastrointestinal side effects develop, or a maximum of 6 mg is taken without relief. Alternatively, to avoid gastrointestinal adverse reactions, intravenous colchicine 2 mg can be given with additional doses of 1 mg at six hourly intervals for a total of 5 mg.

When gouty arthritis is suspected diagnostic maneuvers should include roentgenography of the joint(s) and needle aspiration of the affected joint with examination of the joint aspirate under polarizing microscopy. While joint aspiration is routine in the differential diagnosis of arthritis, common disorders such as gouty arthropathy continue to be overlooked in the midst of major therapeutic regimens such as immunosuppression for organ transplantation. It should be kept in mind that acute gout in a transplant recipient may occur in the presence of a normal serum uric acid level (Case 2), a normal joint radiograph (Case 3), and/or the absence of detectable joint fluid (Case 3).

REFERENCES

1. Tiller DJ, Hall BM, Horvath JS, et al: Gout and hyperuricemia in patients on cyclosporin and diuretics. *Lancet* 1985; 1:453.
2. Palestine AG, Jussenblatt RB, Chan CC: Side effects of systemic cyclosporine in patients not undergoing transplantation. *Am J Med* 1984; 77: 652–656.
3. Lin JY, Rocher LL, McQuillan MA, et al: Cyclosporine-induced hyperuricemia and gout. *N Engl J Med* 1989; 321:289–292.
4. West C, Carpenter BJ, Hakala TR: The incidence of gout in renal transplant recipients. *Am J Kidney Dis* 1987; 10:369–372.
5. Hande KR, Noone RM, Stone WJ: Severe allopurinol toxicity: description and guidelines for prevention in patients with renal insufficiency. *Am J Medicine* 1984; 76:47–54.
6. Kahl LE, Thompson ME, Griffith BP: Gout in the heart transplant recipient: physiologic puzzle and therapeutic challenge. *Am J Med* 1989; 87:289–294.
7. Scott JT: Drug-Induced gout. *Baillieres Clin Rheumatol* 1991; 5:39–60.
8. Gores PF, Fryd DS, Sutherland DE, et al: Hyperuricemia after renal transplantation. *Am J Surg* 1988; 156:397–400.
9. Venkat-Raman G, Sharman VL, Lee HA: Azathioprine and allopurinol: a potentially dangerous combination. *J Intern Med* 1990; 228:69–71.

Supraventricular tachycardia induced by swallowing

LAWRENCE GOULD, MD

Cardiac arrhythmias that occur on swallowing liquids or solids are a very uncommon condition. This entity was first described in 1926.¹ However, the mechanism that causes these arrhythmias is still unclear. There have been a number of case reports describing these arrhythmias in patients with no cardiac disease and normal esophageal function. We report a patient who has underlying cardiac disease and an esophageal diverticulum, in whom supraventricular tachycardia only develops on swallowing.

CASE REPORT

A 38-year-old woman first had supraventricular tachycardia in November 1990, while swallowing food. She subsequently had six episodes of supraventricular tachycardia related to swallowing various foods. She had no other gastrointestinal symptoms.

The patient has Eisenmenger's syndrome with a ventricular septal defect and anomalous venous return. In spite of this disorder, she works full time, and her only symptoms have been decreased exercise tolerance for approximately two years. She also has a long history of exertional cyanosis. She has been on digoxin, 0.125 mg daily, for many years.

The physical examination revealed a blood pressure of 140/80 mm Hg with a regular pulse rate of 90 beats/min. There was minimal cyanosis of the lips, mucous membranes, and finger tips. The carotid pulsations were normal. There was a severe thoracolumbar scoliosis. The lung fields were clear to auscultation with good breath sounds bilaterally. There was a grade III/VI harsh holosystolic murmur over the left precordium, with an accentuated pulmonic component of the second heart sound. There was no hepatosplenomegaly or peripheral edema.

The electrocardiogram showed a sinus rhythm with a S1, S2, S3 pattern, with a QR in lead VI compatible with right ventricular hypertrophy. The chest film showed mild cardiomegaly, with a prominent main pulmonary artery segment. The pulmonary artery markings were increased centrally with peripheral tapering, consistent with pulmonary arterial hypertension.

A recent echocardiogram showed a large membranous ventricular septal defect. There was significant right ventricular hypertrophy. There was no subpulmonic or valvular pulmonic stenosis. The main pulmonary artery was enlarged, and the valve motion was consistent with pulmonary hypertension. There was azygos continuation of the inferior vena cava so that the hepatic veins directly entered the right atrium. There was also a bilateral superior vena cava draining into the coronary sinus. The Doppler examination showed bidirectional shunting at the level of the ventricular septal defect. There was also a moderate degree of pulmonic regurgitation.

The hemoglobin count was 15.5 g/dL with a hematocrit of 45.9%. A gastrointestinal series was within normal limits except for the presence of a pulsion type diverticulum in the midesophagus.

The patient sought treatment for cardiac arrhythmia at the emergency rooms of various hospitals. An electrocardiogram demonstrated a supraventricular tachycardia of 200 beats/min. Intravenous administration of verapamil proved to be effective in terminating the arrhythmia. She subsequently found that pressure on the eyeballs could stop the cardiac arrhythmia. She was placed on oral verapamil, 40 mg three times per day. This drug was efficacious, and she has not had a recurrence of the arrhythmia for four months.

DISCUSSION

In a recent review of the literature, Morady et al² found that the supraventricular tachycardia induced by swallowing has certain clinical features. The patients are usually males between the ages of 45 to 75 and in most cases there is no heart disease or disorders of the esophagus. The cardiac arrhythmia lasts less than 30 seconds. The palpitations occur on swallowing liquids or solids and can even accompany dry swallowing.

The present case is unique in that the patient is a 38-year-old woman with severe congenital heart disease. Furthermore, she has a pulsion-type diverticulum of the midesophagus.

The supraventricular tachycardia provoked by swallowing is more often an atrial

From the Department of Medicine, The Methodist Hospital, Brooklyn, NY.

Address correspondence to Dr Gould, The Department of Medicine, The Methodist Hospital, 508 6th St, Brooklyn, NY 11215-9008.

tachycardia and less frequently atrial fibrillation.² In most cases, the atrial tachycardia was due to an automatic focus.²⁻⁴ However, Yeh et al⁵ reported that during electrophysiologic studies in their patient, swallowing consistently induced premature atrial beats, initiating a sustained atrioventricular reentry tachycardia, incorporating a retrograde, conducting, left-sided accessory pathway.

Schroeder et al⁶ demonstrated that swallowing reliably provoked an automatic atrial focus type of tachycardia that usually changed into an atrioventricular nodal reentry tachycardia when a critical delay in atrioventricular nodal conduction was achieved.

The mechanism by which swallowing produces the supraventricular tachycardia remains speculative. Some authors have suggested a mechanical stimulation of the left atrium by the distended esophagus.^{7,8} However, this mechanism appears unlikely for the following reasons: the tachycardia can be provoked by dry swallowing; the tachycardia focus may be in the high right atrium or interatrial septum, which is not adjacent to the esophagus; and balloon inflation in the esophagus at the level of the atria may not provoke the tachycardia.^{2,6}

The enlarged atria, in the present case, may have played a role in predisposing to the tachycardia. However, this is only conjecture.

The most likely mechanism by which swallowing can initiate the supraventricular tachycardia is a neural reflex. The

afferent and efferent branches of the vagus nerve are activated during swallowing. Preferrential vagal discharge to the atrial myocardium could result in atrial ectopic activity without bradycardia. Therefore, one possible mechanism of supraventricular tachycardia induced by swallowing is activation of the excitatory vagal efferent to the atria.

Suarez et al⁹ suggest that there is a vagal-related shortening of the atrial refractory period in normal fibers, co-existing with delayed conduction in the affected atrial fibers. This will produce an intra-atrial micro-reentry with a resultant atrial tachyarrhythmia.

Digitalis has not been successful in controlling tachyarrhythmias. There are also reports that cardiac glycoside therapy can exacerbate tachycardia.^{6,8} The most effective antiarrhythmic drugs for suppressing supraventricular tachycardia have been procainamide,⁶ disopyramide,¹⁰ and quinidine.^{2,11} These drugs have been used alone or in combination with a beta blocker or a calcium blocker. There are a number of reports documenting the beneficial action of the calcium blocker. There are a number of reports particularly documenting the beneficial action of the calcium blocker, verapamil.^{2,3}

In one case, antiarrhythmic drugs were not successful in controlling the tachycardia, and the patient subsequently underwent successful surgical ablation of an accessory pathway with abolition of the sustained tachycardia.⁵ In another patient, a circular esophageal myotomy at the junc-

tion of the middle and lower third was performed to interrupt vagal afferents from this portion of the esophagus. The procedure reduced the frequency of palpitations.¹²

REFERENCES

1. Sakai D, Mori F: Uber einen Fall von Sog "Schluchtachycardie." *Z Gesamte Exp Med* 1926; 50: 106-109.
2. Morady F, Krol, RB, Nostrant TT, et al: Supraventricular tachycardia induced by swallowing: a case report and review of the literature. *Pace* 1987; 28:555-560.
3. Terasaka R, Takemoto M, Haraoka S: Swallowing induced paroxysmal supraventricular tachycardia. *Jpn Heart J* 1987; 28:555-560.
4. Ransbottom, JC, Mirro MJ: Refractory swallowing induced paroxysmal supraventricular tachycardia. *Clin Cardiol* 1988; 11:51-52.
5. Yeh SJ, Fu M, Lin FC, et al: Paroxysmal supraventricular tachycardia initiated by a swallowing induced premature atrial beat. *J Electrocardiol* 1986; 19:193-196.
6. Schroeder DP, Wooley CF, Leier CV: An electrophysiologic study of swallowing induced tachycardia. *Chest* 1978; 74:314-317.
7. Bajal SC, Ragaza EP, Silva H, et al: Deglutition induced tachycardia. *Gastroenterology* 1971; 62:632-635.
8. Engel TR, Laporte SM, Meister SG, et al: Case studies: tachycardia upon swallowing: evidence for a left atrial automatic focus. *J Electrocardiol* 1976; 9:69-73.
9. Suarez LD, Chiozza MA, Foye R, et al: Swallowing dependent atrial tachyarrhythmias: their mechanism. *J Electrocardiol* 1980; 13:301-305.
10. Bexton RS, Nathan AW, Hellestrand KJ, et al: Paroxysmal atrial tachycardia provoked by swallowing. *Br Med J* 1981; 282:952.
11. Lindsay AE: Tachycardia caused by swallowing: mechanisms and treatment. *Am Heart J* 1973; 85:679-684.
12. Kalloor GJ, Singh SP, Collis JL: Cardiac arrhythmias on swallowing. *Am Heart J* 1977; 93: 235-238.

Morgagni hernia mimicking a lipomatous tumor

PERRY S. GERARD, MD; ERIC WILCK, MD; ELLIOT SENDEROFF, MD; STUART GOLBEY, MD

Herniation of omentum into the thoracic cavity may result in an enlarging chest mass. When bowel loops are present within the hernia, the diagnosis can often be made on a plain film. If this is not possible, the ability of computed tomography (CT) scans to differentiate between various densities and to define anatomic structures can help distinguish Morgagni hernias from other causes of intrathoracic masses. We present a case of massive herniation of omentum through the foramen of Morgagni with no evidence of bowel in the hernia on either plain films or CT scan.

CASE REPORT

A 45-year-old, obese woman was referred to this hospital with a diagnosis of an enlarging right pericardial mass. The mass was initially detected on a pre-employment chest radiograph obtained six years before admission. Further evaluation of the mass with repeat chest films concluded that it was a pericardial cyst, and the patient's condition was managed conservatively.

The patient remained asymptomatic until shortly before referral to this hospital, when she developed a persistent dry cough associated with right-sided chest pain. There was also a sense of fullness in her right chest. Follow-up chest radiographs (Figs 1,2) showed enlargement of the mass occupying the anterior mediastinum adjacent to the right heart border. CT scan of the chest demonstrated that the mass was of fat density and contained serpentine linear densities consistent with fibrotic strands or blood vessels (Fig 3). Slices obtained through the region of the liver

showed an abnormal fat density situated between the anterior abdominal wall and the margin of the liver. Lower scan images showed colon adjacent to the mass. The colon appeared displaced anteriorly and superiorly.

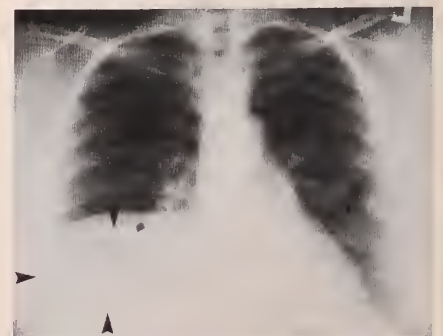


FIGURE 1. Posteroanterior chest radiograph shows a sharply defined mass at the right base obliterating the right heart border (arrowheads).

From the Departments of Radiology (Drs Gerard, Wilck, and Golbey) and Surgery (Dr Senderoff), Maimonides Medical Center, 4802 Tenth Ave., Brooklyn, NY.

Address correspondence to Dr Gerard, Department of Radiology, Maimonides Medical Center, 4802 Tenth Ave., Brooklyn, NY 11219.



FIGURE 2. Lateral film of the chest shows an anterior mass (arrowheads).

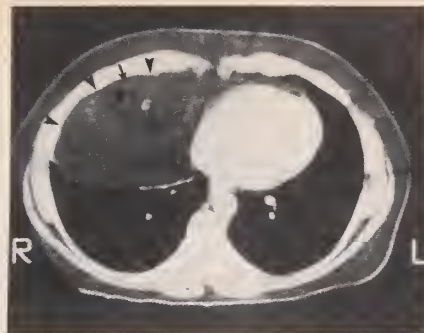


FIGURE 3. CT Scan of the chest demonstrates an anterior mass of fat density (arrowheads) containing fibrotic strands and vessels (arrows).

Differential diagnoses of a liposarcoma or a Morgagni hernia were entertained.

The patient's symptoms continued, and she underwent surgery. A right lateral thoracotomy was performed. An encapsulated, fatty mass was identified and subsequently separated from the pericardium; its origin was traced to a defect in the anterior diaphragm. The abdomen was then opened, and a defect in the diaphragm was palpated where peritoneum and omentum had herniated through the foramen of Morgagni. When the intrathoracic specimen that contained omentum was excised, it weighed two pounds. There was no evidence of any visceral organs in the hernia sac. The patient made an uneventful recovery.

DISCUSSION

Anterior diaphragmatic hernias have been noted as early as 1761, when Giovanni Morgagni described the entity on the basis of a large autopsy study.¹ The defect most commonly occurs slightly lateral to the xiphoid, although it may also occur in a directly posterior position. The etiology of this defect is thought to be failure of fusion of the diaphragm to the costal cartilages and sternum.²

Morgagni hernias are associated with obesity, aging, trauma, and other causes of

increased intra-abdominal pressure. Morgagni hernias usually occur on the right side, since the heart and pericardium cover left-sided defects. Omentum and transverse colon are the most common structures within the hernia sac, although liver and stomach, or small intestine may also herniate. Patients are usually asymptomatic, although complaints of abdominal and retrosternal pain, nausea, vomiting, or dyspnea may occur.^{3,4} Strangulation of bowel within the hernia sac is a rare complication.

The characteristic features of Morgagni hernias have been described with a variety of radiologic imaging modalities, including CT and magnetic resonance imaging (MRI). Several features consistent with the diagnosis include a pericardial fat density, linear densities radiating from the parasternal aspect of the diaphragm consistent with blood vessels, and an abnormally high location of the diaphragm.³ MRI has the added advantage of depicting the diaphragmatic defect directly in the coronal and sagittal plane.⁵

Morgagni hernia is often forgotten in the differential diagnosis of large intrathoracic

and mediastinal masses when obvious intra-abdominal organs are not present. The differential diagnosis includes entities such as pericardial cyst, large fat pad, lipoma, liposarcoma, or other neoplasm. Radionuclide liver scans have been reported to be useful in cases in which the herniated sac contains liver.⁶ The diagnosis is often made when bowel loops are visualized in the hernia sac on an abdominal radiograph or barium enema examination. Even if no bowel is present within the sac, tenting of the bowel superiorly can suggest the diagnosis.⁷

Surgical repair can be performed via a thoracic or transabdominal approach.⁷ The key to all methods of repair is to reduce the content of the hernia, excise the hernial sac completely, and close the defect in the diaphragm to prevent future recurrences.

This case provides an unusual presentation of an uncommon entity. Progressive herniation of omentum through the defect resulted in a large intrathoracic mass. In spite of the massive herniation of omentum, there was no evidence of bowel within the hernia at the time of CT or laparotomy.

REFERENCES

1. Kelly KA, Bassett DL: An anatomic reappraisal of the hernia of Morgagni. *Surgery* 1964; 55: 495-499.
2. Paris F, Tarazona V, Casillas M, et al: Hernia of Morgagni. *Thorax* 1973; 28:631-636.
3. Fagelman, D, Caridi JG: CT diagnosis of hernia of Morgagni. *Gastrointest Radiol* 1984; 9:153-155.
4. Schneidau A, Baron HJ, Rosin RD: Morgagni revisited: A case of intermittent chest pain. *Br J Radiol* 1982; 55:238-240.
5. Yeager BA, Guglielmi GE, Schiebeler ML, et al: Magnetic resonance imaging of Morgagni hernia. *Gastrointest Radiol* 1987; 12:296-298.
6. Comer TP, Schmalhorst WR, Arbogast NR: Foramen of Morgagni hernia diagnosed by liver scan. *Chest* 1973; 63:1036.
7. Thomas TV: Subcostosternal diaphragmatic hernia. *J Thorac Cardiovasc Surg* 1951; 63:750.

Transitional cell carcinoma of the renal pelvis in an incompletely duplicated collecting system

DANILO ASASE, MD; RONALD G. FRANK, MD; PERRY S. GERARD, MD; KRIS LINDSAY, MD; GILBERT J. WISE, MD

Primary tumors of the renal pelvis and collecting system are relatively uncommon,

comprising about 7% of all renal tumors and less than 1% of all genitourinary tumors.¹ Duplication of the renal pelvis and ureters is one of the more common urinary tract anomalies,² although neoplasms encountered within this anomaly are rare.³

We present, to the best of our knowledge, the first case of a primary transitional cell carcinoma of the renal pelvis in an incompletely duplicated collecting system.

CASE REPORT

A 66-year-old man was admitted with a three-day history of painless gross hematuria associated with progressive weakness and near collapse at home. His urologic history dated back approximately two years, with an isolated episode of painless hematuria which he chose not to have evaluated. He denied easy bruising or prolonged bleeding. There was no history of sickle cell disease. He had smoked one pack of cigarettes a day for 15 years.

From the Department of Urology, Coney Island Hospital (Dr Lindsay) and the Departments of Urology (Drs Asase, Frank, and Wise) and Radiology (Dr Gerard), Maimonides Medical Center, Brooklyn, NY.

Address correspondence to Dr Gerard, Department of Radiology, Maimonides Medical Center, 4802 Tenth Ave., Brooklyn, NY 11219.



FIGURE 1. Intravenous urogram demonstrating contrast filling the upper pole segment of the left kidney (arrows) with nonvisualization of the lower pole segment.

His medical history was otherwise unremarkable.

On physical examination, the patient's temperature was within normal limits, blood pressure was 110/60 mm Hg; and pulse was 98/min. The abdomen was soft, with no palpable masses. There was no costovertebral tenderness. The external genitalia were normal, and the prostate was mildly enlarged.

Laboratory results on admission were significant for a hematocrit of 16.7%. The blood urea nitrogen and creatinine levels were within normal limits. The coagulation profile, including the bleeding time, were within the acceptable range. Urinalysis confirmed the presence of blood. A plain film of the abdomen revealed multiple pelvic phleboliths. An intravenous urogram demonstrated non-visualization of the middle and lower pole collecting systems of the left kidney suggestive of a possible duplicated left collecting system with obstruction of the lower pole moiety (Fig 1).

A renal ultrasound revealed an enlarged left kidney with hydronephrosis of the lower pole. A double collecting system was seen with an echogenic irregular mass within the distended lower pole renal pelvis. For further evaluation, cystoscopy was performed. A single right and left ureteral orifice was noted situated in normal position, with blood effluxing from the left orifice. No masses were seen in the bladder. A left retrograde ureteropyelogram outlining the lower pole segment showed an abrupt cut-off with an irregular contour of the proximal left lower pole ureter (Fig 2). Percutaneous transfemoral renal angiography demonstrated a hypovascular lower pole left kidney segment.

The patient underwent a left nephroureterectomy with resection of a cuff of bladder. A polypoid cauliflower-like mass was identified filling the lower pole collecting system (Fig 3). Pathologic examination confirmed duplication of the collecting system with papillary transitional cell carcinoma grade II/IV in the lower limb of the duplex system. Distal ureteral fusion was noted. A follow-up cystoscopic examination at three months failed to reveal recurrence within the bladder.

DISCUSSION

Primary tumors of the renal pelvis and collecting system are relatively uncommon

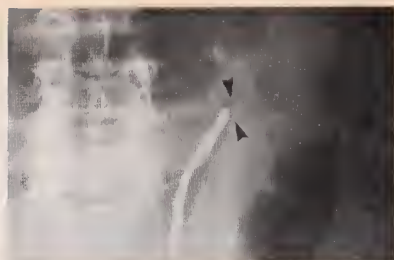


FIGURE 2. Left retrograde ureterogram demonstrating obstruction of the proximal lower pole ureter (arrows).

when compared with tumors of the renal parenchyma. They comprise about 7% of all renal neoplasms and less than 1% of all genitourinary tumors. The majority of these tumors are urothelial in origin. The relative incidence of transitional cell carcinoma is 51:3:1 for the bladder, renal pelvis, and ureter, respectively.¹

Complete duplication of the renal pelvis and ureters, although one of the more frequently encountered urinary tract anomalies, is only found in about 1 in 125–150 autopsies.² Most individuals with duplicated systems remain completely asymptomatic and the anomaly is never discovered. Incomplete ureteral duplication with a common ureteral stem entering the bladder results from bifurcation of the ureteral bud after it has taken its origin from the mesonephric duct. Except for the so-called "yo-yo reflux," with an increased association with urinary tract infection and pyelonephritis, this anomaly is rarely of clinical significance.

The finding of a primary urothelial carcinoma in one of a pair of ureters in a duplicated collecting system has been previously reported on a number of occasions.^{4–6} In contrast, the presence of primary urothelial carcinoma of the renal pelvis in a completely duplicated system has only been reported on a single occasion.³ In that case, cystoscopy revealed grossly bloody efflux from the lowermost ureteral orifice, and the tumor was localized in the upper pole moiety of a right kidney unit.

The accurate urologic diagnosis of transitional cell carcinoma of the renal pelvis depends on a number of complementary imaging modalities. The intravenous urogram may enable the earliest possible identification of a filling defect. Lowe and Roylance⁷ have categorized five distinct urographic patterns seen on intravenous urography associated with pelvic-filling defects. Similarly, the presence of the stipple sign represents the appearance of contrast material insinuating within the tumor fronds.⁸ Retrograde pyelography may provide detailed mapping of the collecting system; that may not have been apparent on intravenous urography.

Sonography may help differentiate renal pelvic filling defects. Unlike calculi, tumors



FIGURE 3. Gross bivalved specimen of the left kidney shows a cauliflower-like mass filling the lower pole of the renal pelvis (arrows).

generally do not produce shadowing. They frequently are less echogenic than fat. At times, they may be confused with blood clots before clot breakdown.

Computed tomography may identify transitional cell tumors of the renal pelvis larger than one centimeter. These tumors are hypovascular and the renal contour is well preserved. Invasion of the renal vein and vena cava have been documented in isolated cases.⁹

Angiography plays a small role in the diagnosis of transitional cell carcinoma of the renal pelvis. These tumors may be hypovascular or occasionally avascular. Similarly, at the present time magnetic resonance imaging does not offer any additional information. Unlike the case of renal pelvic transitional cell carcinoma previously reported, the tumor described in this case report was localized to the lower pole of an incompletely duplicated collecting system.

REFERENCES

1. Richie JP: Carcinoma of the renal pelvis and ureter, in Skinner D, Lieskovsky O (eds), *Diagnosis and Management of Genitourinary Cancer*. WB Saunders Co., 1989, pp 323–336.
2. Perlmuter AD, Retik AB, Bauer SD: Anomalies of the upper urinary tract, in Walsh PE, Gittes RF, Perlmuter AD, and Stanley TA (eds), *Campbell's Urology*. Philadelphia, WB Saunders Co., 1986, pp 1665–1759.
3. Budd JS: Primary transitional cell carcinoma of renal pelvis in a duplicated collecting system. *Br J Clin Pract* 1987; 41:1063–1064.
4. Banya Y, Abe T, Sasaki H, et al: A case of primary ureteral carcinoma in the duplicated renal pelvis and ureter diagnosed by transurethral uretero-renaloscopy. *Hinyokika Kyo* 1986; 32:453–461.
5. Kurnom H, Nanbu K: A case of primary ureteral carcinoma in the duplicated ureter. *Rinsho Hinyokika* 1981; 35:486–471.

6. Tudor RG, Clear JD: Conservative surgery in the management of carcinoma in a duplex ureter. *J R Coll Surg Edin* 1986; 31:323-324.
7. Lowe PP, Roylance J: Transitional cell carcinoma of the kidney. *Clin Radiol* 1976; 27:503-512.

8. Mclean GK, Pollack HM, Banner MP: The "stipple sign" urographic harbinger of transitional cell neoplasms. *Urol Radiol* 1979; 1:177-179.

9. Gatewood OB, Goldman SM, Marshall FF, et al: Computed tomography in the diagnosis of transitional cell carcinoma of the kidney. *J Urol* 1982; 127:876-887.

FROM THE LIBRARY

TREATMENT OF CANCER OF THE CERVIX

The main purpose of external x-ray therapy in the treatment of carcinoma of the cervix is to supplement the radiation given by radium to the parametrium and the nodes draining the cervix. In almost all instances the amount of radiation administered centrally by the intracavitary radium is adequate and cancerocidal. Therefore, when administering external radiation, one should attempt to spare the midline structures, while treating the lateral pelvis adequately. In addition, most of the complications of the radiation treatment of carcinoma of the cervix are due to the effects of excessive radium dosage on the sensitive structures (rectosigmoid, bladder, and small intestine). This is a second reason for attempting to spare the midline when external roentgen therapy is applied.

In the average radiology department or office, x-rays of 200 to 250 kilovolts are available for therapy. Moderately heavily filtered beams should be used. There is a difference of opinion as to the proper sequence for x-ray therapy. In this medical center radium is administered first, followed in approximately one week by a five-week course of external therapy. There are three exceptions to this program:

A grossly infected lesion or a patient with pelvic inflammatory disease is given roentgen therapy first (in an attempt to irradiate the infection).

A cervix grossly distorted by cancer and in which the external os cannot be identified is irradiated with x-rays preliminary to radium insertion.

A patient with a severely bleeding lesion receives external x-ray therapy initially.

We use long narrow anterior and posterior fields 18 by 20 cm. average size, separated 4 cm. at the midline. In addition, oblique posterior sacrosclatic fields are applied.

A minimal tissue dose of 3,500 r to the lateral pelvic wall is given in five weeks.

It should be emphasized that the treatment plan must be adjusted to the individual patient. Thick heavy patients require larger doses in order to obtain similar tissue doses.

In planning external therapy we find it wise to expose x-ray films with the therapy cones in place upon the patient. These films guarantee accurate x-ray beam direction. The location of the ports should be clearly marked upon the patient's skin to ensure similar treatment at each visit.

With the plan outlined above, very little radiation sickness occurs. The skin reaction is not usually severe.

ROBERT O. LOOMIS, MD; MARIO PRIOLETTI, MD;
ALFRED S. BERNE MD; CHESTER E. CLARK, MD
(*NY State J Med* 1955; 55:3480-3484)

Address correspondence to Editor, New York State Journal of Medicine, 420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication after editorial review. All letters are personally acknowledged by the Editor.

The value of the *New York State Journal of Medicine*

TO THE EDITOR: I have just read the October issue of the *Journal* from cover to cover and want you to know how much I enjoy each issue. I was delighted to read the Australian adventure of Elizabeth Kavalier, which you made possible, and the report on Leonardo's anatomical drawings convinced me to make a trip to Philadelphia to see the exhibit at the Museum of Art. I thank you and congratulate you on having made the *Journal* both medically instructive and culturally enriching.

ALFRED GELLHORN, MD
Director of Medical Affairs
State of New York Department of Health
Empire State Plaza
Albany, NY 12237

Distress over attempts to discontinue the *New York State Journal of Medicine*

TO THE EDITOR: I am distressed to learn that serious consideration is being given in some quarters to ceasing publication of the *New York State Journal of Medicine*, a step that, in my opinion, would tragically undermine the stature of the Medical Society of the State of New York.

I do not have to tell you that the *Journal* has an enviable reputation and many of its scholarly articles have been cited in the medical literature over the past century. Furthermore, it is an important updating reference source for the medical students who are members of the Medical Society.

The *Journal* does much to maintain and enhance the prestige of the Society, and it is incredible that its value to our medical organization is not recognized by some seemingly powerful individuals of limited vision.

If publication of this important journal is straining the finances of the Society, perhaps we need to change our advertising representatives. In any event, the *Journal* is a high-priority item, in my view, and it may well be that the Society can divest itself of less important and more costly activities and services without causing the degree of injury we would suffer by abandoning the *Journal*.

Please be assured that many of us firmly support your efforts to keep the *Journal* alive. I, for one, am withholding payment of the

1993 dues until I feel confident that the *Journal's* existence is no longer threatened.

ABRAHAM L. HALPERN, MD
Clinical Professor of Psychiatry
New York Medical College
720 The Parkway
Mamaroneck, NY 10543-4299

The need to continue publishing the *New York State Journal of Medicine*

TO THE EDITOR: Apparently, over the past several months, some within the Medical Society of the State of New York (MSSNY) have been advocating termination of publication of the *New York State Journal of Medicine* and replacing it with a socio-economic medical tabloid publication. This proposal was alluded to by Dr Milton Gordon, Chairman of the Committee on Publications, Library and Archives in the July issue of the *Journal*.¹ Dr Gordon and other members of the Publications Committee wisely opposed this proposal.

The *Journal* is unique in New York State as the only peer-reviewed clinical and scientific journal published primarily for physicians of this state. It is also among the leading journals of this country, ranked among the top 5% of peer-reviewed medical journals by the National Library of Medicine.¹ Loss of this important publication would be a further step in the denigration of the academic standing of New York medicine. The death of this prestigious and historic journal, added to the State's loss of leadership in such medical issues as obtaining National Institutes of Health funding for biomedical research, will further sap the vitality of New York State's once preeminent position in American medicine.

Socio-economic issues are important and need to be covered in some form of publication. Many organized medical groups such as the American College of Physicians and the American Medical Association cover these socio-economic issues in newspapers. However, they continue to publish major peer-reviewed clinical and scientific journals. Some organizations use a brisk newsletter format as the vehicle for communicating to society members about medical socio-economic issues. Others use insert sections in their clinical journals. None of these should replace publication of the *Journal*.

The *Journal* is highly rated, widely respected, and serves the needs of the majority of MSSNY members as was documented in a 1987 readership survey.² I urge the Society to

continue publishing this important journal, which serves as a critical link to practicing physicians, academicians, medical students, and house officers.

RICHARD D. LEVERE, MD
Professor and Chairman
Department of Medicine
New York Medical College
Valhalla, NY 10595

1. Gordon M: An update on the *New York State Journal of Medicine*. *NY State J Med* 1992; 92:295-298.
2. Imperato PJ: Readership survey of the *New York State Journal of Medicine*. *NY State J Med* 1987; 87:606-612.

High regard for the *New York State Journal of Medicine*

TO THE EDITOR: I was astonished and distressed to hear that there is consideration of abandoning publication of the *New York State Journal of Medicine* and producing a throw-away tabloid in its stead. It is difficult for me to square such a course of action with my impression of the Medical Society of the State of New York (MSSNY) as a forward-looking medical society.

One of the reasons that I participate actively in MSSNY affairs is my high regard for the *Journal*. Although I cannot claim close knowledge of all state medical society publications throughout the country, the *Journal* stands out in my mind as distinctly superior to those with which I am familiar. The idea of abandoning it for a throw-away publication is both puzzling and shocking.

Much as I value my membership and active participation in MSSNY, abandonment of the *Journal* would send a message throughout the medical community that would cause me—and, I suspect, many other physicians—to reconsider the value of MSSNY membership.

I hope MSSNY will reaffirm its commitment to the high quality that has characterized the *Journal* in recent years.

PETER ROGATZ, MD
76 Oakdale Lane
Roslyn Heights, NY 11577

Praise for the quality of the *New York State Journal of Medicine*

TO THE EDITOR: It has recently come to my attention that the Medical Society is debating whether or not to continue publication of the *New York State Journal of Medicine*.

It would be very sad to witness the disappearance of a journal with the standing that the *New York State Journal of Medicine* has enjoyed since its first appearance in 1901.

In randomly glancing over the Miner Library's 92-year run of the *Journal*, it can hardly be argued that its scholarly content is lower now than it once was or that the *Journal* enjoyed a prestige earlier in the century that it no longer has. The scholarly content of the *Journal* has been consistently high, whether directed toward regional health issues or topics of general scientific interest.

The *New York State Journal of Medicine* does not have to be another *New England Journal of Medicine* to justify its publication. The *Journal* always has and should continue to provide a forum for the discussion of Medical Society business and health issues in New York State, as well as provide a medium for the publication of research coming out of the State's many centers of medical research.

As a medical librarian and historian of medicine, I would be very sorry to see a periodical with such a long publishing history and of such consistent quality disappear or be transformed into a monthly throwaway.

CHRISTOPHER HOOLIHAN

History of Medicine Librarian

Edward G. Miner Library

University of Rochester Medical Center

601 Elmwood Avenue

Rochester, NY 14642

Support for the *New York State Journal of Medicine*

TO THE EDITOR: I am writing to express my appreciation and support for the *New York State Journal of Medicine*.

As you can see from my return address, those of us on the West Coast are avid readers of the *Journal*. It represents a broad spectrum of stimulating articles, dealing with timely, provocative issues. Furthermore, it presents both articles of scientific interest and those that profile individuals or attitudes that are at the core of the healing process.

I further commend the *Journal* for its high standards of review for each article, thus assuring the quality and accuracy of all that appears in its pages.

I commend you for your excellent editorship of this fine publication, and I sincerely hope that it will continue to appear in its present, valuable format.

RABBI LEVI MEIER, PhD

Chaplain/Psychologist

Cedars-Sinai Medical Center

8700 Beverly Boulevard

Los Angeles, CA 90048-1869

Support for continuing the *New York State Journal of Medicine* as a peer-reviewed clinical and scientific publication

TO THE EDITOR: The *New York State Journal of Medicine* has been continuously published as a peer-reviewed clinical and

scientific journal for 92 years. I have recently learned that there are some in the Society leadership who would like to discontinue the *Journal* or else transform it into a socio-economic tabloid. This would be a serious mistake in my view. Numerous society members that I know are high in their praise of the *Journal* and find it of great value, as do I. We already receive so many throw-away tabloids and do not need yet another one.

Most members consider the *Journal* as the main benefit of membership. It helps to retain members and to recruit young physicians. The high quality of its content gives the Society great respect and national visibility that cannot be matched by many state medical societies.

The *Journal* should not only be continued as a peer-reviewed scientific and clinical publication, but also strengthened. I greatly value it and wish to express my strong support for it.

BERNARD J. PISANI, MD

Past-President

Medical Society of the State of New York

153 West 11 Street

New York, NY 10011

Thanks from the Committee on Publications, Library, and Archives for support of the *New York State Journal of Medicine*

TO THE EDITOR: On behalf of the Committee on Publications, Library, and Archives, I want to thank Drs Gellhorn, Halpern, Levere, Pisani, Rogatz, Mr Hoolihan, and Rabbi Meier for expressing their appreciation and strong support of the *Journal*. We are also grateful to the many others who have written or telephoned to express their support of the *Journal* and to tell us of its great value to them.

As the committee that oversees the publication of the *Journal*, we fully agree with these assessments of the publication's quality and its value to the society's membership. So do the majority of society members, according to a readership survey conducted for us a few years ago.

There are some in the society leadership who would like to transform the *Journal* into a throwaway or else discontinue it altogether. Although we respect the right of these individuals to hold this view, we strongly disagree with it. We also disagree with their wish to remove the society from all educational activities of a scientific and clinical nature and to transform it into an organization uniquely focused on socio-economic issues.

I want to assure society members and other readers that the Committee on Publications, Library, and Archives is doing its best to support the continued publication of the *Journal*.

MILTON GORDON, MD

Chairman, Committee on Publications,

Library, and Archives

Medical Society of the State of New York

420 Lakeville Road

Lake Success, NY 11042

Regulated medical waste: Is any of it infectious?

TO THE EDITOR: I read with interest Sean F. X. Dugan's article "Regulated medical waste: Is any of it infectious?" which appeared in the August issue of the *Journal*.¹ The author should be commended for having carefully collected and documented the necessary evidence.

It is troubling, given the facts, that the law in question should have been passed, and it is even more troubling that rules and regulations about the collection and transportation of medical waste should be enforced without any consideration as to cost and effectiveness.

I am mystified by the author's reference to a "sunset provision." From where I sit, the rules and regulations are in place and are more oppressive than ever. I for one have closed my office. Since I cannot fight the law, I put myself in a position where I do not have to comply with it.

From a larger perspective this law is the end result of a failure by the legislature to legislate after due deliberation. Laws are passed without debate in response to perceived fears by the public. These laws are then fleshed out by bureaucrats whose only purpose seems to be to establish and entrench themselves. They write reams of regulations without any thought about their long-term effects.

What is even more worrisome is the fact that once a law is passed it is almost impossible to repeal it and terminate all of the bureaucrats who have been nurturing it. A typical example is the Delaney Clause, which was passed without debate as a rider on another piece of legislation. It simply states that no carcinogen should be added to foodstuffs. This is deceptively simple and demonstrates ignorance about the facts. Yet even after 25 years, no one has had the courage to propose a repeal (even a modification would be a help).

ANTONIO BOBA, MD

587 Albany Post Road

PO Box 631

Hyde Park, NY 12538

1. Dugan S: Regulated medical waste: is any of it infectious? *NY State J Med* 1992; 92:349-352.

In reply. The disposal of regulated medical waste was a Federal issue in New York, governed by the Medical Waste Tracking Act of 1988. This Act had written into it a "sunset provision." This simply means that the legislature that enacted that Act wrote into the body of the Act the date on which it would cease to govern. In this case, that date was June 1, 1991. In fact, on June 1 the Medical Waste Tracking Act of 1988 did expire pursuant to this "sunset provision."

That is not to say that the disposal of medical waste is no longer regulated. To the contrary, it is heavily regulated on the state, county, and even city levels in New York State.

The rules and regulations Dr Boba refers to in his letter to the editor are those promulgated by the Occupational Safety and Health Administration (OSHA), which rules went

into effect in July 1992. The intent of these regulations, issued by a regulatory agency of our government, is essentially to protect people from the viruses that cause hepatitis and AIDS. I do agree with Dr Boba that this extremely voluminous, burdensome, expensive regulatory scheme is entirely unnecessary; the Centers for Disease Control suggestions referable to universal precautions are proven to be effective. These totally unnecessary OSHA regulations are needlessly burdening physicians, hospitals, and dentists, are gigantically costly to implement, and have absolutely no increased incidence of health or safety associated with their implementation. As exemplified by Dr Boba, the medical profession has reacted strongly to these regulations, which carry fines for violations of same. It is probable that these fines will not be covered by any insurance carried by the physicians, and thus will come directly out of the physicians' pockets in after-tax dollars.

On the federal level, the President's Council on Competitiveness, Old Executive Office Building, Room 286, Washington, DC 20501, should be strongly urged by all concerned to look into this wasteful mismanagement of scarce resources. The Environmental Protection Agency Office of Solid Waste, 401 M Street, SW, OS-330, Washington, DC 20460, is responsible for studying the management of regulated medical waste. Michelle Wilson, a lawyer in that office, should also be advised of the scientific and medical evidence that so clearly indicates that there is no danger that people who come in contact with non-sharp regulated medical waste have any higher incidence of infection than does the general public.

Finally, rather than abandoning the issue to the bureaucrats and legislators referred to in Dr Boba's correspondence, physicians, medical centers, clinics, dentists, and others

adversely affected by these regulations could join the political process to educate our legislators, so they apply the appropriate political pressure necessary to relieve the profession of this onerous burden. The medical profession has succeeded in this political arena on other occasions. For instance, our State Office of Court Administration advises that 14,224 medical malpractice suits were filed statewide in our supreme courts in 1986. The medical profession rallied, and brought political pressure to bear on the issue. Last year, only 3,410 medical malpractice suits were filed in the supreme court system statewide. This clearly demonstrates that our state political system does respond to appropriate pressure.

SEAN F. X. DUGAN, LL.M.
Martin, Clearwater & Bell
220 East 42 Street
New York, NY 10017

New Literary Journal in Medicine to be Published

Mediphors a literary journal of the health professions will publish its first issue in March 1993. The editors of *Mediphors* are inviting submissions in the following categories: poetry, humor, commentary, fiction, and general articles. The topics should have some relation to medicine and health but may be quite broad. For author instructions and subscription information, contact *Mediphores*, PO Box 327, Bloomsburg, PA 17815.

Medical writing

Medical Writing: A Prescription for Clarity. By Neville W. Goodman and Martin B. Edwards with cartoons by Andy Black. 190 pp, illustrated. New York, Cambridge University Press, 1992. \$14.95 (softcover)

There was a time when the only book available on medical writing was the classic and rather dull tome of Morris Fishbein, the legendary editor of the *Journal of the American Medical Association* of half a century ago.¹ Since then, the subject has become fair game, with subsequent contributors subject only to the judgment of readability and credibility. Now, we try again. Yet another book has been written about improving one's capacity to turn out a medical paper acceptable not only to journal editors but to the immutable and oft-violated laws of science, logic, and communication. This volume, *Medical Writing: A Prescription for Clarity*, comes from our more learned colleagues across the sea, whose umbilical ties to the English language remain purer and more generic than those here in the colonies.

My initial interest in the prospect of a new book on medical writing quickly succumbed to the rather more cynical and downright oppositional thought, "Oh, dear, not another useful book that will never be read by those who need it the most!" In addition, would it not induce American authors to start affecting British spelling, "colourfully, whilst still internes," the way college kids returning from a summer in Europe cross their 7s? It seemed to me that the best book on the subject, Robert A. Day's *How to Write and Publish a Scientific Paper*, had already been written and not so far back as to require either an update or a significant competitor.² What could compare with Michael Crichton's classic piece in the Sounding Board section of the *New England Journal of Medicine* on the uses of medical obfuscation?³ The primary author of this small but compact paperback, a British anesthesiologist and medical editor, thoughtfully provided a cartoonist whose work was sufficiently clever for me to agree to review the book.

My natural bias was to hope that the definitive Holy Book on the subject had finally been revealed, particularly as the Oxford University Press has been putting out books for over 450 years, and one can count on them to know a good book, rather than one that will merely sell. However, it was hard to stay optimistic when the dedication (to sweethearts? to teachers?) was couched solely in the very abbreviations (SEG, RWT, NWG, and so forth) we all deplore, and in unexplicated references (to Quiller-Couch, for example, an estimable gentleman whose name will most certainly be unfamiliar to all save those who majored in English literature in college).

Nor was that all. In the introduction, the traditional, impassioned plea for brevity, clarity, and simplicity (BCS) was made. On the very next page, in the first paragraph of Chapter Two, up came the following, which I for one had to read three times fully to comprehend: "If doctors write descriptions of clinical trials that confuse readers assumed to be of equal knowledge and understanding, then that is the responsibility of the writers not the readers, who might justifiably wonder whether the conduct of the clinical trials had been similarly confused." I am not sure whether to say, "It takes one to know one," or "Those who can't, teach," but since both are more

mean spirited than I should like to be, I withdraw both. Instead, I refer us all to the elegant writings of Sir Thomas Browne, for example, *Um Burial* or *Nosce Teipsum*. In these physician-written, 17th century works we will find no BCS, (and no BS, for that matter), but rather long, complex, and exquisitely crafted masterpieces of English sentences, all of which demand that the reader have an attention span longer than ten words.

I have never understood why prose must have BCS. Will we never shake the influence of that wretched fisherman Hemingway?! Does this emphasis not presuppose that the reader hasn't the intelligence or perseverance to find the end-sentence period, no matter where it may turn up? Is this worship of BCS so patronizing as to assume that the average medical writer has not the capacity to control and reign in his sentences so that they will not escape and break their own legs like runaway horses? I, for one, am delighted by a well-expressed Baroque roundabout and lose heart at the Dick and Jane approach to medical writing. Writing it well is not the same thing as keeping it short.

Overcoming impulsive and intuitive bias, I persevered. Please understand that it takes discipline and training for a reviewer to endure being objective throughout an entire book, when less than (fewer than?) five minutes into the task, she is, as the teenagers say, "turned off." But patience is a virtue (let's hear it for the cliché), and in no time the authors gave enough signs of self-redemption to raise my flagging hopes.

I applaud their emphasis on demystifying, unravelling, and forthwith disposing of the elephantine, obscurantist, and untutored Byzantine style affected by traditional scientific writing. Taking back good prose from the research scientists is always a worthy goal, and one to which I will drink any time. (Or should I say, "Spirits fermentii may be imbibed in exhibiting the approval ratings elicited by the data presented?") The authors are fierce proponents of the clear thinking upon which rests the foundation of all good writing. Tirelessly, they point out common fallacies in logic that undermine the credibility of many scientific presentations, and reiterate the need to avoid the pitfalls that invalidate conclusions. I'll imbibe to that, too.

It will not surprise you if I mention that my heart soon began to go out to these most sincere of authors, for their noble and Quixotic attempt to encourage medical scientists to write in downhome English instead of Medibabble, a cause as worthy as the promulgation of Esperanto and just about as hopeless. Why do they bother? I loathe my own cynicism, but I simply cannot imagine any practicing physician caring enough about his syntax to find the time to study this or any other such book, much less read our review, write down the necessary details of purchase, and scurry or send a secretary scurrying to a book store to tote it home. My heart tells me that sales will be relegated to libraries, those great repositories of personal vanity and unread classics, where the book will turn yellow alongside definitive treatises concerning the toxicology of South American island plants, or the manual of first aid for the French armies engaged in the Great War.

I know whereof I write. Having read the manuscripts submitted to this *Journal* for at least five years, relishing some,

raging at occasional others, groaning over many, and wading somnambulistically through stacks of trivia significant to but a few, I know how loudly authors squawk when asked to do the most elementary of re-writes on their impenetrable papers. Editorial pleas that they weed their verb gardens are flicked away like pesky mosquitoes. Often we must don the gloves ourselves and grobble in the muck until the papers come to flower. I do indeed applaud any attempt by the authors to clean up the messy writing to which I have become accustomed. Believe me, it would give me pleasure to award them the rave review, to make them stars, to send them to the West Coast and the media talk shows where the great messages of American society originate! But I can't imagine who would care enough to read this book, besides an occasional virginal junior attending with an eye for an academic career, and hoping against hope to find a pearl to enable cracking the ultimate medical publishers in New England the first time out. However, the elusive quest for objectivity prevailed. My goal was to overcome my ambivalence about the ultimate utility of this book, instead of pointing out what I liked and didn't like about it, and letting the reader/buyer ultimately to make his own decision.

Now, here's an example of what bothers me. The authors prefer "Cocaine causes addiction" to the more circumlocutious, "It has been shown that cocaine causes addiction." They insist it means the same thing and that the active rather than the passive voice should prevail for punch and clarity. This is the standard message of reformists. However, is it true? "Cocaine causes addiction" is a pithy remark, but it smacks of opinion and oversimplification. "It has been shown that . . ." at least implies that studies have been done to confirm the statement, and the presentation of bibliographic references should be *de rigueur* in support of this. I am not convinced that both sentences really do mean the same thing. Have we not gone overboard in our rejection of the elegant passive voice? Yet how can we not want to give an affectionate squeeze to two men (and their clever pictorial partner), who are so keen to get the lead out of medical writing, they would substitute "before" for "prior to," as in "Kiddy, please go and wash your hands prior to eating lunch?"

The authors are not talking trivia here when they advocate the use of the active voice rather than the passive, and recommend rephrasing "The rats were injected" with "I injected the rats." I believe they fail to consider the awesome psychic significance of giving up the passivity universal in scientific reporting. If people wanted to report what they had done in forthright, responsible prose, they would long since have done so. In fact, given the narcissistic propensities of many major researchers, the very failure to present the material as coming from one's own hand has great meaning. If rats were injected, the blame can always be placed on others: colleagues, technicians, or persons unknown. Once an author has committed himself to "I injected the rats," he has painted himself into a corner. The bold and naked confession "I did" evokes primitive and carly images of childhood, from which most learned persons would wish to escape. The voice of the bad mother returns: "You injected the rats?! You wretched, miserable child! How many times have I told you never to inject the rats?! Let me see your hands. Go wash immediately. The next time I catch you injecting the rats you will have no chocolate pudding for dessert." Dear British cousins, save your breath! The doctors of this country will never respond to your logic. Yours is the voice of the all-knowing father, intent on raising a child properly and teaching him his P's and Q's. It will

avail you naught. (Or should I said "zed"?) Those who mail in manuscripts were born to rebel against father as well as mother, both of whom are embodied in the awesome person of the medical editor, the unforgiving judge and critic.

The authors regard as an integral whole the performance of scientific work and the reporting of it, stressing the need for honesty and clarity in both. Strange to say, not every book on medical writing is willing to take this difficult step across the boundary between the purity of the original study and the way in which it is later presented to others. In other words, GIGO prevails in the world of medicine as well as computers. The authors are wise to remind the reader that an acceptable paper embodies more than the turn of a clear phrase.

Having stated their belief that much of today's medical writing is poor and tainted, they move on to give their remedies. Subsequent chapters start to sound more familiar, not that much removed philosophically from the elements of English grammar which should have been mastered long since by those who publish. (Remember that classic adult refresher course, often called "The Little Book," Strunk and White's, *The Elements of Style*?) Their chapter headings are "Guidelines to Clearer Writing," "Is There a Better Word?," "Superfluous Words," "Trouble with Short Words," "Consistency: Numbers and Tenses," "Word Order and Pronouns," "Punctuation," and "Constructing Sentences." The authors include a chapter of examples of abominable writing, each of which have been corrected. The final chapter includes more hideous examples which the reader is asked to correct in person. An index and generous references are included. The cartoons are charming.

Particularly lacking from a book so recently published is any discussion of the medical or scientific journal itself, and the electronic revolution now taking place, which may one day render the term "written word" obsolete. The traditional medical journal is almost a threatened species, and with it the reporting formats that have prevailed since the 17th century. That's something to think about.

There are few among us eccentric enough to peruse books on how to write as a hobby and competition for the time of the needy researcher/publisher is heavy duty. Therefore, I would not recommend this book as the one reference to keep handy. I do recommend Robert Day's book, which I have just reread, and which I find pertinent, comprehensive, and so light hearted as to be a joy to read for it's own sake. For those interested in non-sexist writing, I suggest *The Handbook of Nonsexist Writing For Writers, Editors, and Speakers*, by Casey Miller and Kate Swift.⁴ For those so phobic, terrified, and avoidant of the writing experience, I suggest a behavior therapist, or, if this form of therapy fails, as it so often does, an authors' editor. For those who sink to the bottom of the barrel like a stone, I can only recommend eschewing a career in academic medicine.

NAOMI BLUESTONE, MD

Consulting Editor

New York State Journal of Medicine

1. Fishbein M: *Medical Writing. The Technique and the Art*. Chicago, Press of the American Medical Association, 1938.

2. Day RA: *How To Write and Publish a Scientific Paper*. Philadelphia, ISI Press, 1979.

3. Crichton M: Medical obfuscation: structure and function. *N Eng J Med* 1975; 293:1251-1259.

4. Miller C, Swift K: *The Handbook of Nonsexist Writing for Writers, Editors, and Speakers*. New York, Lippincott and Crouse, 1980.

SURGICAL ATTENDING ROUNDS

By K. Francis Lee, MD, and Cornelius M. Dyke, MD. 393 pp. Philadelphia, Lea & Febiger, 1992. \$27.50 (softcover)

This book, designed particularly for students and residents in surgery, attempts to duplicate the educational values of surgical attending rounds by presenting short case reviews followed by questions and answers as though a professor were asking the questions and a student or resident were supplying the answers. However, in this situation the reader of the book is reviewing the author's attempt to answer his own questions, and thus, there is less stimulus to learning. Furthermore, this format is only partially successful in duplicating approaches to patient care found in the live "professor's rounds." In addition, the case presentations themselves are relatively short and do not match the intellectual challenge that a live patient with real problems does.

In spite of these qualifications, the residents have done a very thorough job in reviewing the literature and in choosing and answering a variety of questions about the surgical problems being discussed. As would be expected, some chapters are much more thorough than others, covering even rare aspects of the problem being discussed.

The 32 chapters have been written by 24 different residents (or recent residents), and in some chapters, there is evidence of the lack of long-term experience and a feel for what is most important and what is relatively unimportant.

Probably one of the most important uses of this book might be as a review for students and residents before upcoming attending rounds. Editing could have been improved. There are many misspellings and typographical errors in every chapter.

The ones most likely to benefit from this book are the residents who spent so much time and effort in selecting the cases, identifying the appropriate questions, reviewing the literature, and coming up with reasonably concise and accurate answers to the questions proposed. Students and residents who use this book will no doubt want to reformulate for themselves questions about the problems presented and coming to their own conclusions about the appropriate answers.

CHARLES D. SHERMAN, JR, MD
Clinical Professor of Surgery
University of Rochester
School of Medicine and Dentistry
Highland Hospital
1000 South Avenue
Rochester, NY 14620

HOMELESSNESS: A PREVENTION-ORIENTED APPROACH

Edited by René I. Jahiel, MD, PhD. 409 pp. Baltimore, MD, The Johns Hopkins University Press, 1992. \$60.00 (hardcover)

Do we need another book on homelessness? Does the grim reality require yet more documentation? The answers are Yes and Yes but only if well crafted; this volume is excellently planned and written to be the last word (perhaps).

Dr Jahiel and his colleagues designed a thorough, critical, and scholarly review of current knowledge on the subject of homelessness. Their prevention-oriented approach is adapted from public health disciplines. As Dr Jahiel describes it, prevention of homelessness and its ill effects can be primary (avoiding it in the first instance), secondary (placing homeless persons in secure, stable homes), or tertiary (minimizing the harmful consequences of homelessness). Furthermore, to achieve this intent we "must have knowledge of the affected individual...and of the physical and social environments...to understand the relative contributions of personal and environmental factors...and the expected impact of interventions..." Thus, this volume.

The book's 18 chapters have been prepared by 26 authors, many well-known for either their hands-on experience in work with homeless persons or research and program development. This volume contains all the information that one might possibly want on the history of homelessness in the United States; the numbers of such individuals and families by the best available evidence; the prevalence of mental disorder; what ethnographic studies offer in explaining behavior, needs, and barriers to help. Concrete and highly specific data are provided. For example, Dr Jahiel's chapter, "Services for Homeless People," considers the following: shelters (number, and cost per year, day, or bed), food programs (meal costs), general health and psychiatric care, alcohol abuse treatment, employment programs, opportunities for education of homeless children, social services case management, and housing.

The overview chapters are supported in further detail by studies of specific programs. These include consideration of the Skid Row Mental Health Services, Los Angeles, and a discussion of social networking in helping homeless persons in St Louis. Gary Blasi, in reviewing the role of legal aid organizations, offers a precise outline of areas for legal advocacy (income maintenance programs, residence, and identification requirements, access for the mentally ill, shelter). He then tells us how to do it.

The book is particularly strong in its section documenting the social context of homelessness. Hamburg and Hopper analyze national trends over the past two decades in household income and composition; characteristics of the housing stock; population shifts; and specific governmental policies affecting income, housing, and the disabled. "It is this cluster of factors, their changes over time, and their reciprocal interaction at any one time that provide the essential background against which crises of dislocation have been played out." This is a succinct, on-target summary of the problem.

Previous attempts to explain and analyze homelessness can justly be faulted because of imprecision, guesswork, and self-serving generalizations by advocates of all stripes. Although this book has its modest faults in repetitiveness, use of jargon, simplistic reasoning, and sermonizing, these venial sins are far more than compensated for by the depth and relevance of the material and the rigor with which it is provided. It is especially valuable that Dr Jahiel both identifies the "...wide gap between what we know of the problem and what we are doing...to prevent people from becoming homeless..." and now, with his co-authors, through this text, designs preventive approaches to homelessness.

PHILIP W. BRICKNER, MD
Chairman, Department of
Community Medicine
St Vincent's Hospital and Medical
Center of New York
153 West 11th St
New York, NY 10011

THE DESIGN AND ANALYSIS OF RESEARCH STUDIES

By Bryan F. J. Manly, 353 pp, Cambridge, England, Cambridge University Press, 1992. \$89.95 (softcover)

Professor Bryan F. J. Manly of the Department of Mathematics and Statistics, University of Otago (New Zealand) set out to write a text "to provide research workers in the biological, health, and social sciences with the background they need in order to collect and analyze data in an intelligent and critical manner." He aims this book to "people who have already mastered the material" which he believes usually is presented in first-level statistics courses "and who are ready and willing to know more about the aspects of statistics that are most likely to be useful to the quantitative researcher."

The book is organized into 11 chapters covering commonly encountered research approaches. These issues include differ-

ences between observational and experimental studies; sample survey designs; assessment of treatment effects; linear and multiple regression; interrupted time/series analysis; and computer-intensive statistical methods. He describes the various analytical procedures with adequate depth. Nine of the chapters contain "examples," which are suggestions for additional thinking about the material presented in the chapter. The illustrations are drawn from a range of areas often outside of either the medical disciplines or the health care domain. However, the bibliography covers appropriate clinical and statistical literature from both the British Commonwealth and the United States. Only one chapter is particularly weak, given other available material. Chapter 10, "Ethical Considerations," seems superficial in terms of research undertaken in any country and may not be applicable to practical and regulatory constraints governing research in the United States at the present time.

Since the title states that the book deals with both the design and analysis of research studies, it is somewhat unbalanced in scope. This is a common flaw among research methods textbooks. The design phase of research involves the conduct of an investigation from its conceptualization and planning through the actual conduct of the study. Data analysis must be planned along with every other aspect. Manly does not deal with the manner in which the researcher progresses from design to analysis. This book still views the analytic stage as its primary focus. This is not a realistic perception. In practice, most researchers learn the planning stage by actually participating in research as students or apprentices, and eventually refine their skills during their own work. A more substantial portion of the text dealing directly with the planning of research and the complexities of study design would have been an important addition. There is a useful chapter, "Synthesis: Carrying Out A Research Study," which is a good overview for beginners seeking to undertake their first independent investigation. However, its placement as the final chapter, coupled to its scant 15 page length, lead to the conclusion that it was an afterthought. It does not reinforce the critical concept that no matter how sophisticated the analytic level, a poorly designed study is destined to fail or yield poor-quality data.

Manly's book is neither a text on medical statistics nor biostatistics. There are various softcover primers on these fields currently available which are directly geared to clinical medicine. Such basic statistics texts generally are poised at a more rudimentary level and contain only passing discussions of many of the subjects dealt with here. It is a reasonable premise that texts addressing the advanced topics covered here usually will not deal only with purely medical material. There also are

more comprehensive hardcover textbooks limiting discussion to specific procedural issues, but these frequently are bogged down in the mechanics of calculation. Manly chooses to remain more distant from the mechanics and deal with the principles. Although, there is a potential shortcoming in this approach, namely that the reader may lack the technical competence to perform the technique, the ideas behind the technique indeed do become clear. Many clinicians may not need more than an understanding of the logic and potential application of the technique; in-house consultants or external collaborators ultimately will perform the work.

This is a practical volume that does not seek to cover the realm of statistical thinking and procedures. No statistical text can satisfy the needs of researchers at every level. Professor Manly has done a highly respectable job of putting together a useful compilation of important aspects of data analysis. However, it is not for the uninitiated. In spite of a literate style, comprehension does require the perspective of some degree of statistical background. Unfortunately, this may be beyond the neophyte who has completed one or two courses. There is a definite audience for this book among practitioners of various disciplines in medicine, public health, and in quantitative specialties of the biological and social sciences. It is a workable supplementary text for advanced masters or doctoral level students and experienced researchers alike.

GARY B. BERINGER, DRPH
Visiting Professor
Department of Preventive Medicine and
Community Health
State University of New York
Health Science Center at Brooklyn
450 Clarkson Ave.
Brooklyn, NY 11203

WHEN MEDICINE WENT MAD: BIOETHICS AND THE HOLOCAUST

Edited by Arthur L. Caplan, PhD. 372 pp.
Totowa, NJ, The Humana Press, 1992.
\$22.50 (hardcover)

This book represents a compilation of presentations made at a University of Minnesota Conference held on May 17-19, 1989, to focus on the following five major themes: What role did mainstream medicine and science play in the creation of the Nazi state; what did German scientists and physicians think about and do in the name of eugenics and euthanasia; what moral rationales were used to justify the involvement of medicine and science with genocide, euthanasia, and racism; should scientists and physicians make any use of information obtained from barbarous experiments conducted on innocent persons in concentration camps; and what is the appropriate use of metaphors and analogies to the Nazi era in contemporary debates in bioethics?

Caplan and others at the conference argued that the racist underpinnings of Nazi ideology were firmly rooted in the racial hygiene theories prominent in German biology during the 1920s and early 1930s, well before Hitler came to power. Nazism was not a philosophy espoused on the fringes of German medicine and science. Rather, it had roots deep in the mainstream of German biology, medicine, and public health.

The Nazis established a program of sterilization and euthanasia under which German physicians murdered countless children and adults. These individuals were considered unworthy of life because they were physically or mentally ill, or socially undesirable (eg, Jews). The Nazi program climaxed at Auschwitz, where doctors chose those who were to die, supervised the killings in the gas chambers, and determined when the victims were dead. Doctors ordered, supervised, and at times carried out the killing of debilitated patients on the medical blocks. At the same time, they kept up a pretense of medical legitimacy by signing false death certificates listing spurious illnesses. Doctors helped determine how many people should be kept alive to fill the slave-labor requirements of the IG Farben enterprise at Auschwitz and gave advice on how to dispose of the enormous numbers of bodies produced by the gas chambers.

At Auschwitz, Jews, Gypsies, and others were sterilized by injection, radiation, or surgery, injected with vaccines made from dental infections, subjected to massive bleedings for blood-group experiments, brainwashed with chemicals, infected with typhus, and exposed to toxic substances. Vivisections were performed, and human flesh was used for culture media as well as the making of lampshades and tobacco pouches.

In sum, doctors supervised the entire killing process at Auschwitz from beginning to end. How were physicians, sworn by oath and conviction to ease suffering, transformed from healers to systematic killers? At the Minneapolis conference, Caplan reviewed the moral rationales advanced by Nazi physicians who administered the euthanasia program, supervised mass genocide, and conducted brutal experiments on Jews and other groups in concentration camps, and who grounded their actions on utilitarian principles. They maintained that the state was justified in sacrificing the minority to advance the interests of the majority; only those "doomed to die" anyway were selected for research involving lethal experiments.

Dr Jay Katz, professor of law at Yale University, reviewed the atrocities perpetrated by Nazi scientists in the name of scientific research. He concluded that the ability to undertake murderous science was grounded in the following five norms: obedience to authority; a commitment to racial superiority; a concern for the security and well-being of the state in time of

war; a belief in the importance of scientific progress; and an ethos of (pseudo) professionalism that held that patients' interests were best served by trusting their doctors. Katz first thought that Nazi data should be used, but after greater consideration, concluded the opposite was correct.

The most emotional part of the conference concerned the ethics of using data obtained from experiments on victims from concentration camps. Dr Robert Pozos argued that Nazi research on hypothermia, although cruel and often fatal, was scientifically sound and the only source of information about exposure to extremely cold temperatures; it should therefore be used. Pozos' position was heatedly and passionately attacked by three survivors of medical experiments at Auschwitz. Dr Robert Berger, Professor of Surgery at Harvard University School of Medicine and himself a survivor of the camps, questioned the scientific validity of the Nazi experiments and the claim that they are the sole source of information about exposure to cold temperatures.

No consensus emerged from the conference about the ethics of using Nazi findings. Nevertheless, no one who reads this book will remain unmoved by the powerful testimonies it offers, and by the illumination of fundamental medical and moral problems that still disturb us today. As a holocaust survivor myself, I have very deep and personal feelings about these problems.

FRED ROSNER, MD
Assistant Dean and Professor of Medicine
Albert Einstein College of Medicine
Bronx, NY
Director, Department of Medicine
Queens Hospital Center Affiliation Long
Island Jewish Medical Center
Jamaica, NY 11432

MARKETING MANAGEMENT ISSUES IN AMBULATORY HEALTH CARE

Edited by Charles D. Schewe, PhD. 198 pp.
Binghamton, NY, The Haworth Press,
1992. \$29.95 (hardcover)

"Marketing," often a misleading substitute for "selling," is a sensitive word when used in conjunction with health care services. Selling health services challenges the ethics of the greater health care community. On the other hand, understanding the needs and perceptions of a target population for health care services is an important planning tool and contributes to a functional society.

We do not know enough about how the public selects ambulatory health care services, or what they think of the services they have received. Although the clinical literature continues to make great strides in uncovering scientific mysteries, we still do not know why a woman chooses to have a mammogram or what she thinks of her doctor. Useful research in the area of marketing ambulatory health care is needed

by many planners and managers who must develop services in a competitive arena where ambulatory-care revenue has eclipsed inpatient revenue at many institutions across the country.

The Haworth Press has addressed this need by publishing the *Journal of Ambulatory Care Marketing* and the book reviewed here. This book was also published as Volume 4, Number 2, 1991 of that journal.

Charles Schewe, PhD, editor of *Marketing Management Issues in Ambulatory Health Care*, has assembled a collection of papers presented at the April 1990 meeting of the American Association for Advances in Health Care Research. In this book, the papers are organized in three sections: "Customer Satisfaction and Service Issues," "Quality and Cost Issues," and "Market Research and an Aging Population." Many of the papers present useful research in these areas.

Measuring patient satisfaction is challenging at best. A patient's response to a questionnaire is often shaped by the timing and location of the data-gathering activity and by the patient's perception of how completion of the questionnaire might affect his or her health care. Several excellent papers in the first section of the book explore this sensitive subject, and rightly call for additional research in this most difficult area.

I found the "Quality and Cost" section less useful. One of the three papers in this section documented employers' health care cost concerns, and one discussed pricing a new health care service.

The final section of this book provided ample evidence of the aging of the American population, and its implications for health-services planning and marketing. These papers join a growing body of literature yet to be translated into significant innovative planning for the health-services needs of this growing population. Special issues that must be addressed when conducting market research among older Americans are described by the authors of one article, and designing transportation for the elderly is the subject of another. As one author states, "There is a paucity of empirical work conducted on the use of and the impact on the elderly consumer resulting from direct marketing strategies and activities." Each of the papers presented here sheds some light on the subject.

This book could increase the reader's knowledge of marketing ambulatory care services. Several of the articles included in this collection are well developed and make a significant contribution to the limited body of knowledge in this important area. However, this book should not be the first source selected on this subject because it does not contain an overview of marketing management issues or concepts and approaches. As a collection of papers, it does not address the topic head on but rather nibbles at its edges.

With this caveat, a number of the papers presented here do contribute to the "...paucity of empirical work..." regarding this subject, and could be useful as a reference.

JAY A. ROBERTS
Director, Clinical Practice Affairs
State University of New York
Health Science Center at Brooklyn
450 Clarkson Ave
Brooklyn, NY 11203

VIOLENCE IN AMERICA: A PUBLIC HEALTH APPROACH

Edited by Mark L. Rosenberg MD, MPP,
and Mary Ann Fenley. 199 pp. New York,
Oxford University Press, 1991. \$32.95
(hardcover)

Rosenberg and Fenley, the editors of this challenging book are to be congratulated. In this volume, they have provided us with an excellent review of current research in the field of personal violence. Most important is the recognition that violence is not inevitable but to be viewed as a public health problem that can be studied, understood, and prevented. It is a problem that no longer will be dealt with exclusively by the criminal justice system. Credit should also be given to our former Surgeon General, Dr C. Everett Koop who sponsored the conference resulting in this book.

The topics for the eight chapters of *Violence in America* have been well chosen and excellently organized. They consist of the "Introduction," "Assaultive Violence," "Child Abuse," "Child Sexual Abuse," "Rape and Sexual Assault," "Spouse Abuse," "Violence Against the Elderly," and "Suicide." What the reader will also appreciate finding are the data sources on the causes, consequences, and prevention of violence in every chapter. The contributors, all prominent and well-known specialists in their fields, convincingly prove what the health professionals are capable of contributing and achieving.

In addition, included here are the controversial and contradictory results of some of the studies. An example of this is the current and accepted thinking that abused children grow up to be abusing adults. This, however, is questioned here so that further research studies are clearly necessary to resolve such contradictory findings. Every chapter will assuredly raise many challenging questions.

This book represents a further step in helping to overcome a problem that society has been struggling with from the beginning of time. It is enthusiastically recommended for all physicians and should be in the library of every medical college.

STEPHEN NORDLICHT, MD
Memorial Hospital for Cancer and
Allied Diseases
200 East 74th St
New York, NY 10021

Guidelines for authors

ORIGINALITY

The *New York State Journal of Medicine* welcomes research papers and original essays on the practice of medicine, medical education, public health, the history of medicine, medicolegal matters, legislation, ethics, the mass media, and socioeconomic issues in health care.

Manuscripts should be prepared according to the "Uniform requirements for manuscripts submitted to biomedical journals" (*NY State J Med* 1992; 92:122-125). The requirements were established by the International Committee of Medical Journal Editors, of which the *Journal* is a participating member. These Guidelines are intended to highlight aspects of the *Journal's* particular style of publication.

A manuscript will be considered for publication if it is original, has not been published previously in whole or in part in either a medical journal or a lay publication, and is not simultaneously under consideration elsewhere. A copy of any possibly duplicative material, such as a reference "in press," should be submitted along with the manuscript.

PREPARATION

An original typewritten or "word-processed" manuscript and two photocopies (to facilitate outside review) are required. If the manuscript is not accepted for publication, the original and one copy will be returned. All figures must be submitted in triplicate. The manuscript should be double-spaced throughout, including references, tables, legends, quotations, and acknowledgments. A separate title page should include the full title of the paper in upper and lower case type, the names of the authors exactly as they should appear in print (including their highest academic degree), and the names of all providers of funding for research on which the paper is based. Information on the amount and allocation of funding is optional.

A corresponding author should be designated in the covering letter. Authors should list their title and affiliation at the time they did the work, and, if different, their present affiliation. The addresses and telephone numbers of all authors should be supplied for editorial purposes. All authors of a manuscript are responsible for having read and approved it for submission.

CATEGORIES

Research Papers should be limited to 3,000 words and should include the following sections: Introduction, Methods, Results, Discussion, and References. Multiple subheadings and numbered lists are discouraged. An abstract limited to 150 words should state the reasons for the study, the main findings, and their implications. Statistical evaluations should be described in the Methods section, and the name and affiliation of the statistician should be included in the acknowledgments if this individual is not listed as a coauthor. Reports of experiments involving human subjects must include a description in the Methods section of the informed consent obtained and a statement that the procedures followed were approved by an institutional research review committee. Anonymity of patients must be preserved. Reports of experiments on animals must note which guidelines were followed for the care and use of laboratory animals.

Case Reports should be limited to 1,250 words. Review Articles should not exceed 3,000 words. Commentaries should be between 1,000 and 1,500 words. Other kinds of original essays should not exceed 2,500 words. A letter of inquiry

should be sent to the editor prior to submitting a Review Article or Commentary.

For Research Papers only, scientific measurements should be given in conventional units, with *Système Internationale* (SI) units in parentheses. Abbreviations and acronyms should be kept to a minimum, and jargon should be avoided. Generic names of drugs should be used instead of brand names.

FIGURES

The submission of color illustrations or slides is discouraged. Only black and white glossy photographic prints or "camera-ready" artwork will be accepted. The *Journal* is unable to provide art services such as the addition of arrows to photographs. A signed consent for publication must accompany photographs in which the patient is identifiable. Illustrations from other publications generally will not be considered. Legends for illustrations should be typed on a separate sheet, and for photomicrographs should include magnification and stain. Each illustration should be lightly marked on the back in pencil with the name of the first author, the number as cited in the text, and an arrow indicating the top. Each set of illustrations should be submitted unmounted in a separate envelope.

Tables should be simple, self-explanatory, and few in number. Each table should be typed double-spaced on a separate sheet.

REFERENCES

References should be limited to the most pertinent. The recommended maximum number of references is 25 for Research Papers and most other original contributions (except lengthier Review Articles), 12 for Commentaries and Case Reports, and six for letters to the editor.

Authors are responsible for the accurate citation of references. Citation of secondary sources is discouraged except where the original reference is unobtainable. Authors may not cite references they have not read, and the use of abstracts as references should be avoided.

References should be indicated in the text by superscript numbers following the name of the author (eg, Smith² reported two cases).

The list of references at the end of the article should be typed double-spaced and references should be numbered in the order in which they appear in the text. When there are three or fewer authors, all should be listed; where there are four or more, the first three should be listed, followed by *et al.* Names of journals should be abbreviated according to *Index Medicus* and underlined.

Samples references:

1. Bowen J: Autoimmune paraneoplastic diseases of the nervous system. *NY State J Med* 1991; 91:2-3.
2. Cotran RS, Kumar V, Robbins SL: *Robbins Pathologic Basis of Disease*, ed 4. Philadelphia, WB Saunders Co, 1989, pp 842-845.

REVIEW

All manuscripts are reviewed by the editors, and most manuscripts are sent to outside referees. Decisions concerning acceptance, revision, or rejection of a manuscript are usually made within three to six weeks. Every effort will be made to assure prompt publication of an accepted manuscript. A galley proof will be sent to the author for approval prior to publication.

Address correspondence to Pascal James Imperato, MD, Editor, *New York State Journal of Medicine*, PO Box 5404, 420 Lakeville Road, Lake Success, NY 11042.

MEDICAL SOCIETY OF THE STATE OF NEW YORK

Schedule of Sessions	71
Officers, Councilors, and Trustees	73
Members of the House	76
Reference Committees	79
Nominating Committee	80
Report of the House Committee on Bylaws	81

HOUSE OF DELEGATES

March 11 through March 14, 1993
Rye Town Hilton Hotel
Rye, New York

SCHEDULE OF SESSIONS

Thursday, March 11, 1993

Opening Session 1:00 p.m.

Friday, March 12, 1993

Reference Committee Hearings 8:30 a.m.–5:00 p.m.

Saturday, March 13, 1993

Second Session 9:00 a.m.

Third Session 1:30 p.m.

Sunday, March 14, 1993

Closing Session 9:00 a.m.

A Guide to the 1993 Annual Meeting

Policy-making in the House of Delegates

This section of the New York State Journal of Medicine is a call to the officers, delegates, and members of the Medical Society of the State of New York to attend the 187th Annual Meeting of the Society and the meeting of its House of Delegates; 279 delegates representing 61 county medical societies, 9 district branches, specialty societies, the hospital medical staff section, 12 medical schools, the young physician, resident physician, and the medical student sections will meet at the Rye Town Hilton, Rye, New York on March 11–14, 1993.

The officers, members of the Council and the Board of Trustees, past presidents of the MSSNY, the Commissioner of the New York State Department of Health, the Past President of the American Medical Association from New York, Gerald D. Dorman, MD; Past Executive Vice-President of the Medical Society of the State of New York, George J. Lawrence, Jr., MD; and Past Deputy Executive Vice-President, Robert J. O'Connor, MD; are also official representatives to the House.

Mandated by the Bylaws of the Society, this section lists the names of elected representatives, delegates who are serving on reference committees, and selections of the Nominating Committee for the election of Officers, Councilors, Trustees and AMA Delegates. Also included are the amendments to the Bylaws which will be considered by the House of Delegates.

Since the House of Delegates is the legislative body of the Society, charged with the general management of the State Society and its affairs, members of the Society are urged to use this information to consult with and advise their representatives. Resolutions introduced by the representatives bring members' concerns to the attention of the entire Society. Representatives not only have the responsibility to present the views of their constituents, but also to inform them of the actions taken by this governing body. The House of Delegates also formulates policy for the Society. No officer, councilor, board, commission, committee, or employee may initiate any policy unless such policy has been expressly approved by the House of Delegates, or by the Council of the Society.

If one were to choose the most important work of the House of Delegates, it would have to be that of the reference committees. Any member of the Medical Society of the State of New York has the right to appear before any reference committee and participate in its deliberations. It is also in the reference committees that people outside of the State Society are asked to give their views. Nonmember physicians, guests or interested observers who wish to express their opinions may, with permission, come before the reference committee and speak to the business of the committee. I strongly urge members to use this forum to express their views.

Seymour R. Stall, M.D., Speaker
House of Delegates

John H. Carter, M.D., Vice-Speaker
House of Delegates

MEDICAL SOCIETY OF THE STATE OF



Officers 1992-1993



Morton Kurtz, MD

Queens
President



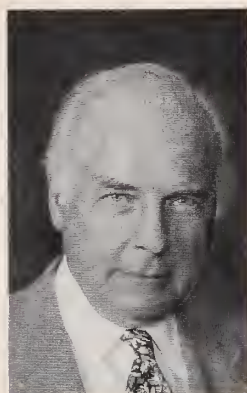
Stanley A. Steckler, MD

Suffolk
President-Elect



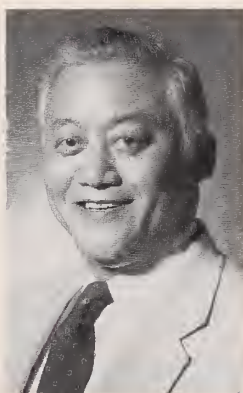
Charles N. Aswad, MD

Broome
Past President



James H. Cosgriff, Jr, MD

Erie
Vice-President



George Lim, MD

Oneida
Secretary



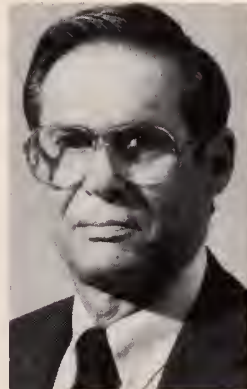
Joyce M. McChesney, MD

Monroe
Assistant Secretary



Antonio F. LaSorte, MD

Broome
Treasurer



Stanley L. Grossman, MD

Orange
Assistant Treasurer



Seymour R. Stall, MD

Dutchess
Speaker



John H. Carter, MD

Albany
Vice-Speaker

Board of Trustees 1992–1993



James M. Flanagan, MD

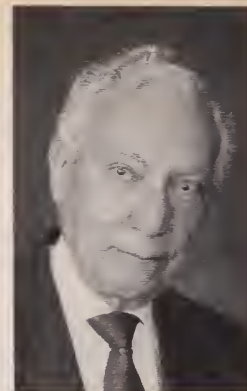
Wayne

Chairman



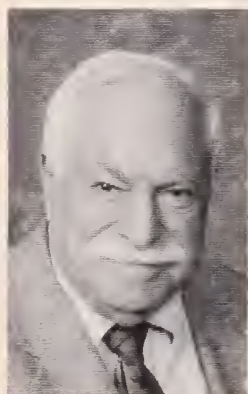
John A. Finkbeiner, MD

New York



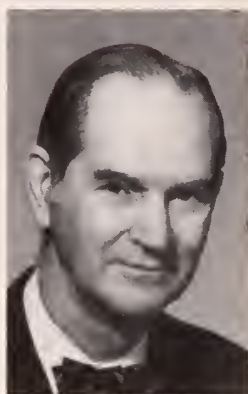
Samuel M. Gelfand, MD

Nassau



M. Theodore Tanenhaus, MD

Kings



Charles D. Sherman, Jr., MD

Monroe



Duane M. Cady, MD

Onondaga



Robert A. Mayers, MD

Westchester

Councilors 1992–1993



Randall D. Bloomfield, MD

Kings



William A. Dolan, MD

Monroe



Robert M. George, MD

Oneida



Stuart I. Orsher, MD

New York



Robert Bruce Bergmann, MD

Nassau



Richard A. Hughes, Sr., MD

Warren



Jeffrey A. Ribner, MD

Broome



Anthony P. Santomauro, MD

Erie



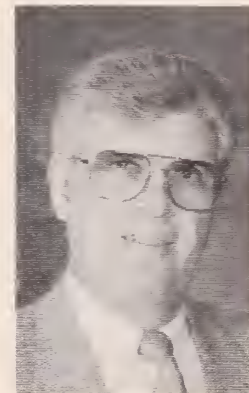
Bruce H. Berlin, MD

Suffolk



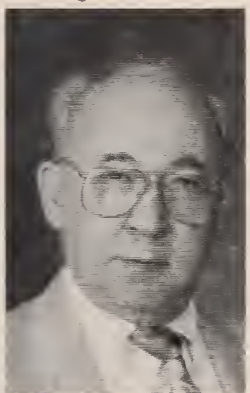
Albert M. Ellman, MD

Albany



Fred N. Flatau, MD

Queens



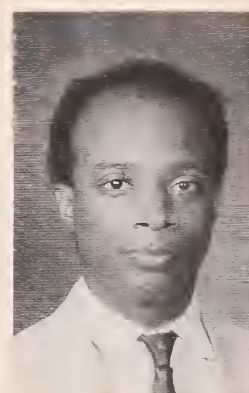
Sanford A. Kaplan, MD

Westchester



Paul Pipia, MD

New York
Resident Physician Councilor



Leon Henderson

New York
Medical Student Councilor

1993 HOUSE OF DELEGATES MEMBERS

The following is a list of members of the 1993 House of Delegates of the Medical Society of the State of New York.

Officers 1992-1993

President—Morton Kurtz, Queens
 President-Elect—Stanley A. Steckler, Suffolk
 Vice-President—James H. Cosgriff, Jr., Erie
 Secretary—George Lim, Oneida
 Assistant Secretary—Joyce M. McChesney, Monroe
 Treasurer—Antonio F. LaSorte, Broome
 Assistant Treasurer—Stanley L. Grossman, Orange
 Speaker—Seymour R. Stall, Dutchess
 Vice-Speaker—John H. Carter, Albany

Councilors

Term Expires 1993

Randall D. Bloomfield, Kings
 William A. Dolan, Monroe
 Robert M. George, Oneida
 Stuart I. Orsher, New York

Term Expires 1994

Robert Bruce Bergmann, Nassau
 Richard A. Hughes, Sr., Warren
 Jeffrey A. Ribner, Broome
 Anthony P. Santomauro, Erie

Term Expires 1995

Bruce H. Berlin, Suffolk
 Albert M. Ellman, Albany
 Fred N. Flatau, Queens
 Sanford A. Kaplan, Westchester

Student Councilor

Term Expires 1993

Leon Henderson, New York

Resident Councilor

Term Expires 1993

Paul Pipia, New York

Trustees

James M. Flanagan, Wayne, *Chairman*
 John A. Finkbeiner, New York
 Samuel M. Gelfand, Nassau
 M. Theodore Tanenhaus, Kings
 Charles D. Sherman, Monroe
 Duane M. Cady, Onondaga
 Robert A. Mayers, Westchester

Past Presidents

1960-1961—Norman S. Moore, Tompkins
 1966-1967—James M. Blake, Schenectady
 1971-1972—George Himler, New York
 1972-1973—Edward Siegel, Clinton
 1975-1976—Ralph S. Emerson, Nassau
 1976-1977—George L. Collins, Jr., Erie
 1978-1979—George T. C. Way, Dutchess
 1980-1981—Ralph M. Schwartz, Kings

1982-1983—Richard D. Eberle, Onondaga
 1983-1984—Bernard J. Pisani, New York
 1984-1985—Allison B. Landolt, Westchester
 1985-1986—Daniel F. O'Keeffe, Warren
 1986-1987—John A. Finkbeiner, New York
 1987-1988—Samuel M. Gelfand, Nassau
 1988-1989—Charles D. Sherman, Monroe
 1989-1990—David M. Benford, New York
 1990-1991—Robert A. Mayers, Westchester
 1991-1992—Charles N. Aswad, Broome

Past Executive Vice-President

George J. Lawrence, Jr., Queens

Past Deputy Executive Vice-President

Robert J. O'Connor, Richmond

Past President of the American Medical Association

Gerald D. Dorman, New York

President of the American Medical Association

John L. Clowe, Schenectady

Commissioner, New York State Department of Health

Mark R. Chassin, MD

District Delegates

(*Elected Delegates of District Branches*)

First—Albert Accettola, Jr, Richmond
 Second—Melvyn Bruckstein, Suffolk
 Third—John A. Ferraro, Rensselaer
 Fourth—Michael Lynch, Washington
 Fifth—George P. Tilley, Onondaga
 Sixth—William E. Clack, Chemung
 Seventh—Norman W. Wetterau, Livingston
 Eighth—Bruce E. Baker, Genesee
 Ninth—Zane A. Miranda, Putnam

Specialty Society Delegates

NYS Soc of Allergy & Immunology—John T. Parrinello, Orange
 NYS Soc of Anesthesiologists—Edward C. Sinnott, Nassau
 NY State Chap Am Coll of Cardiology—Joseph Lauterstein, Sullivan
 NYS Soc of Dermatology—David Sibulkin, New York
 NY Chap Am Coll of Emergency Physicians—
 NYS Academy of Family Physicians—Elise Korman, Suffolk

NYS Soc for Surgery of the Hand—
 NYS Soc of Internal Medicine—Robert M. Kohn, Erie
 NYS Neurosurgical Soc—Herbert Oestreich, Westchester
 Am Coll of Obstetricians & Gynecologists—Robert J. Kaplan, Suffolk
 NY Occupational Medical Assoc—William Schneider, New York
 NYS Ophthalmological Society—Francis J. Gilroy, Broome
 NYS Soc of Orthopaedic Surgeons—Leo Arthur Green, Queens
 NYS Soc of Otolaryngology—Romeo C. Solon, New York
 NYS Soc of Pathologists—Edward C. Zaino, Nassau
 Am Acad of Pediatrics—
 NY Soc of Physical Med & Rehabilitation—Irvin Kotkin, Queens
 NY Reg Soc of Plastic & Reconstructive Surgery—Arthur J. Wise, Nassau
 NYS Psychiatric Assoc—Edward Gordon, Westchester
 NYS Radiological Soc—Jerome Zwanger, Nassau
 NYS Soc of Surgeons, Inc—Theodore C. Max, Oneida
 NYS Urological Society, Inc—P. Miller Ashman, Monroe

Delegates from Component Medical Societies

Albany (5)

Teresa S. Briggs, Albany
 Steven M. Parnes, Albany
 James H. Puleo, Albany
 Nathan P. Reed, Albany
 Demostene Romanucci, Latham

Allegany (1)

Paul Kolisch, Friendship

Bronx (10)

John P. Albanese, Bronx
 Sana Bloch, Bronx
 Neil Calman, New York
 Simeon Carvajal, Demarest
 Hugo Morales, Bronx
 Narayan Pai, Bronx
 Venkatachala Pathy, Bronx
 Anthony Pisacano, Bronx
 Raul Pohorille, New Rochelle
 Juana Toporovsky, Bronx

Broome (4)

Jerome Cohen, Johnson City
 Louis W. Giordano, Endicott
 Roy D. Gill, Johnson City
 Charles Rubin, Johnson City

- Cattaraugus (1)*
- Cayuga (2)*
Richard J. Freeman, Auburn
C. Richard Nangle, Auburn
- Chautauqua (2)*
- Chemung (2)*
Donald Brooks, Elmira
David R. Graham, Elmira
- Chenango (2)*
Evan S. Morrison, Norwich
Lawrence J. Rosenblum, Norwich
- Clinton (2)*
- Columbia (2)*
- Cortland (1)*
- Delaware (1)*
Gary Preiser, Walton
- Dutchess (4)*
Florian M. Cortese, Hyde Park
Reuben Delgado, Fishkill
Eleanor C. Kane, Poughkeepsie
Jagdish Wadhwa, Poughkeepsie
- Erie (9)*
Richard J. Buckley, Amherst
Amy P. Early, Williamsville
Edmond J. Gicewicz, Getzville
Allen L. Lesswing, Williamsville
William K. Major, Jr., Buffalo
Nancy H. Nielsen, Orchard Park
Richard M. Peer, Buffalo
H. John Rubinstein, Kenmore
David O. Scamurra, Kenmore
- Essex (2)*
- Franklin (2)*
William Latrielle, Malone
Charles C. Gibbs, Saranac Lake
- Fulton (1)*
- Genesee (1)*
Cezina Rocha-Lidder, Batavia
- Greene (1)*
Karuvath Enu, Hudson
- Herkimer (2)*
Krishna K. Vadlamudi, Ilion
- Jefferson (2)*
Louis C. Battista, II, Watertown
David O. VanEenenaam, Watertown
- Kings (19)*
Joseph C. Amico, Brooklyn
Rubin Berlinerblau, Brooklyn
Norman S. Blackman, Brooklyn
George W. Calvosa, Brooklyn
Duncan W. Clark, Brooklyn
Clifford Cohen, Brooklyn
Vashti Curlin, Brooklyn
Harold L. Eichler, Brooklyn
Paul Finkelstein, Brooklyn
Robert E. Gordon, Valhalla
Julius Holtzman, Garden City
Martin Markowitz, Brooklyn
Rufus A. Nichols, Brooklyn
Hubert S. Pearlman, Brooklyn
Judithann Pryce, Brooklyn
Abdul Rehman, Brooklyn
Veronica C. Santilli, Brooklyn
Calvin J. Simons, Brooklyn
- Lewis (1)*
John C. Herrman, Lowville
- Livingston (1)*
Sheppard Arluck, Geneseo
- Madison (1)*
Leonard A. Argentine, Oneida
- Monroe (7)*
Marilyn R. Brown, Rochester
Thomas E. Cardillo, Victor
William A. Kern, Jr., Rochester
Joseph F. Kurnath, Rochester
Edward D. Lewis, Rochester
Alexander L. Strasser, Rochester
Edward C. Tanner, Rochester
- Montgomery (2)*
- Nassau (11)*
Patrick F. Carone, Rockville Centre
Sidney Mishkin, Fort Salonga
A. Philip Fontanetta, Mineola
Paul A. Hamlin, Great Neck
Sharon C. H. Mead, Massapequa
Felix A. Monaco, Rockville Centre
Daniel J. Nicoll, New York
John A. Ostuni, Freeport
E. John Pesiri, Massapequa
Neal A. Skolnick, Rockville Centre
Leonard S. Weiss, Levittown
- New York (23)*
Arnold L. Bachman, New York
Melvin H. Becker, New York
Robert S. Bernstein, New York
Michael B. Brodin, New York
Kenneth H. Brookler, New York
Joseph B. Cleary, New York
Anthony A. Clemendor, New York
Irwin J. Cohen, New York
Joseph E. Davis, New York
Joseph C. Dreyfus, New York
George Hyams, New York
Virginia Kanick, New York
Albert B. Knapp, New York
Samuel H. Madell, New York
Aaron G. Meislin, New York
- Alfred F. Moldovan, New York
Donald A. Morris, New York
Donna B. O'Hare, New York
Richard N. Pierson, Jr., New York
Edward W. Powers, III, New York
William B. Rosenblatt, New York
Clifford N. Spingarn, New York
- Niagara (3)*
Mary Ann Bishara, Lewiston
Robert J. Reszel, North Tonawanda
Raymond J. Tuoti, Williamsville
- Oneida (4)*
James D. Dunda, Rome
Kenneth K. Kim, Utica
Steven Z. Kussin, Utica
Timothy H. LaFont, Utica
- Onondaga (7)*
Armand J. Cincotta, Liverpool
Daniel L. Dombroski, Syracuse
Daniel S. Fuleihan, Syracuse
Richard A. Konys, Syracuse
Frank J. Piper, Syracuse
Patricia A. Randall, Syracuse
Jeffrey S. Sneider, Baldwinsville
- Ontario (2)*
W. Bradley Simmons, Canandaigua
Kenneth Steadman, Geneva
- Orange (4)*
Fritz Beauboeuf, Middletown
Stanley F. Brunn, Port Jervis
Clayton R. DeHaan, Middletown
James V. DiLorenzo, Jr, Newburgh
- Orleans (1)*
David B. Meza, Albion
- Oswego (1)*
Corliss A. Varnum, Oswego
- Otsego (3)*
John O. Lusins, Oneonta
David L. Rayfield, Cooperstown
Jonathan W. Sastic, Oneonta
- Putnam (2)*
- Queens (16)*
Marvin L. Blumberg, Rego Park
Daniel Chansky, Forest Hills
John W. V. Cordice, Jr., St. Albans
Daniel G. Deckler, Richmond Hill
Fred S. Fensterer, Glendale
Lorraine M. Giordano, Jamaica Estates
Victor Guarnieri, Bayside
Nicetas H. Kuo, Great Neck
Maxwell J. Marder, Great Neck
Irving B. Margolis, Jamaica
John D. Monteleone, Ozone Park
Frank Ratner, Flushing
Hilda Ratner, Beechurst
Sheldon D. Sax, Flushing
Ralph E. Schlossman, S. Ozone Park
Bernard M. Zazula, Kew Gardens

Rensselaer (3)

Arsenio G. Agopovich, Watervliet
Anthony Troitino, Troy
William A. Whyland, Troy

Richmond (4)

Robert Bonvino, Staten Island
Zoltan Brody, Staten Island
Tano S. Carbonaro, Staten Island
Mark Jarrett, Staten Island

Rockland (4)

Roy H. Lieberman, New City
Stanley H. Oransky, Bardonia
Paul Mercurio, New City
Michael Rader, New City

St. Lawrence (1)

Saratoga (3)

Allen T. Jones, Saratoga Springs

Schenectady (3)

William Busino, Jr., Schenectady
Richard H. Lange, Schenectady
Robert Kennedy, Schenectady

Schoharie (1)

Frederick Michel, Cobleskill

Schuyler (1)

Seneca (1)

Ann Birch, Seneca Falls

Steuben (2)

Suffolk (11)

Stephen I. Braitman, Islip Terrace
Clive D. Caplan, Islip Terrace
Frank R. Collier, Port Jefferson

Nicholas P. Craig, Port Jefferson
Kenneth B. Levites, W. Sayville
Martin Matalon, Bay Shore
Gerard F. Ryan, Patchogue
Robert A. Scher, Huntington
L. Arne Skilbred, Southampton
Jay B. Stambler, East Islip
William H. Weir, Jr., Riverhead

Sullivan (2)

Tioga (2)

Tompkins (2)

Robert A. Hesson, Ithaca
Phillip L. Harris, Ithaca

Ulster (3)

John Anderson, Port Ewen
Stephen L. Hermele, Kingston
John V. Ioia, Kingston

Warren (3)

Robert Hughes, Queensbury
Fred Scialabba, Glens Falls

Washington (1)

Barney Rubenstein, Cambridge

Wayne (3)

David T. Hannan, Newark
Daniel J. Koretz, Ontario
Norman R. Loomis, Ontario

Westchester (9)

Paul S. Carton, Yonkers
Ann C. Cea, Rye Brook
Mark L. Fox, Bronxville
Thomas A. Lansen, Valhalla
Robert C. Mickatavage, Rye
Stephen O. Schwartz, White Plains
Robert L. Soley, White Plains

Pellegrino J. Tozzo, New Rochelle
William J. Walsh, Jr., White Plains

Wyoming (1)

Aurora Gochoco, Warsaw

Yates (1)

Medical School Delegates (12)

Albany Medical—
Albert Einstein College of
Medicine—Melvin Zelefsky, Bronx
Columbia Univ Coll of Phys &
Surg—Linda D. Lewis, New York
Cornell University Medical College—
Mount Sinai School of Medicine—
New York Medical College—Susan A.
Kline, Westchester
New York University of Medicine—
SUNY Health Science Center at
Brooklyn—Pascal Imperato, Kings
SUNY at Buffalo School of
Medicine—Dennis A. Nadler, Erie
SUNY at Stony Brook School of
Medicine—Dorothy S. Lane, Suffolk
SUNY Health Science Center at
Syracuse—
Univ of Rochester Sch of Med—Philip
P. Bonanni, Monroe

Medical Student Delegates (3)

Piers Barker, New York
Jeff Powell, Bronx
Joseph S. Valenti, Erie

Resident Membership Delegate (1)

Mitchell Miller, Albany

Young Physician Delegate (1)

Joseph R. Sellers, Schoharie

Hospital Medical Staff Delegate (1)

L. P. Hinterbuchner, Kings

REFERENCE COMMITTEES

Bylaws

Joseph R. Sellers, MD, Young Physician Section,
Chairperson
Clayton R. DeHaan, MD, Orange
Paul A. Hamlin, MD, Nassau
Frederick J. Michel, MD, Schoharie
Bert Rappole, MD, Chautauqua
Cezina Rocha-Lidder, MD, Genesee (Observer)

Governmental Affairs and Legal Matters

Edmond J. Gicewicz, MD, Erie, *Chairperson*
Jerome Cohen, MD, Broome
Judithann Pryce, MD, Kings
James H. Puleo, MD, Albany
Edward C. Sinnott, MD, New York State Society of
Anesthesiologists
Anthony M. Pisacano, MD, Bronx (Observer)

Hospital and Medical Facilities

Ladislav P. Hinterbuchner, MD, Hospital Medical Staff
Section, *Chairperson*
E. John Pesiri, MD, Nassau
Nathan Reed, MD, Albany
Gerard F. Ryan, MD, Suffolk
Melvin Zelefsky, MD, Albert Einstein College of Medicine
Michael Rader, MD, Rockland, (Observer)

Public Health and Education

Ralph Schlossman, MD, Queens, *Chairperson*
Robert Hughes, MD, Warren
Robert J. Kaplan, MD, American College of Obstetricians
and Gynecologists
Donna B. O'Hare, MD, New York
Edward C. Tanner, MD, Monroe
Phillip L. Harris, MD, Tompkins (Observer)

Reports of Officers and Administrative Matters

Ann C. Cea, MD, Westchester, *Chairperson*
Richard J. Freeman, MD, Cayuga
Linda Lewis, MD, Columbia University College of
Physicians and Surgeons
Rufus A. Nichols, MD, Kings
David L. Rayfield, MD, Otsego
Joseph S. Valenti, Medical Student Section (Observer)

Socio-Medical Economics

Louis Giordano, MD, Broome, *Chairperson*
Kenneth H. Brookler, MD, New York
Tano S. Carbonaro, MD, Richmond
Patricia A. Randall, MD, Onondaga
Robert A. Scher, MD, Suffolk
Evan S. Morrison, MD, Chenango (Observer)

CONVENTION COMMITTEES

Credentials

Florian Cortese, MD, Dutchess, *Chairperson*
Charles C. Gibbs, MD, Franklin
Robert M. Kohn, MD, New York State Society of Internal
Medicine
Richard N. Pierson, Jr., MD, New York
William J. Walsh, Jr., MD, Westchester
Jeffrey S. Powell, Medical Student Section (Observer)

Rules and Order of Business

Mary Ann Bishara, MD, Niagara, *Chairperson*
Eleanor C. Kane, MD, Dutchess
Roy H. Lieberman, MD, Rockland
Venkatachala Pathy, MD, Bronx
David Shulan, MD, Third District Branch
Carol Ellis, MD, New York Occupational Medical
Association (Observer)

Sergeant at Arms

Steven M. Parnes, MD, Albany, *Chairperson*
Michael B. Brodin, MD, New York
William Clack, MD, Chemung
Edward Griffin, Jr., MD, Cattaraugus
Corliss A. Varnum, MD, Oswego
Frank Ratner, MD, Queens (Observer)

Tellers

Norman W. Wetterau, MD, Seventh District Branch,
Chairperson
Teresa S. Briggs, MD, Albany
James D. Dunda, MD, Oneida
Amy Early, MD, Erie
Mitchell Miller, MD, Resident Physician Section
John A. Anderson, MD, Ulster (Observer)

NOMINATING COMMITTEE

To the House of Delegates, Ladies and Gentlemen:

In accordance with Article XI, Section 2 of the Bylaws of the Medical Society of the State of New York, the Nominating Committee met at the Society's headquarters, 420 Lakeville Road, Lake Success, New York, on Thursday, November 19, 1992 at 2:00 p.m.

Members of the Committee present were:

Member-at-Large—**Charles N. Aswad, M.D.**, Broome *CHAIRMAN*

First District Branch—**Ralph E. Schlossman, M.D.**, Queens

Second District Branch—**Samuel H. Gelfand, M.D.**, Nassau

Third District Branch—**Albert M. Ellman, M.D.**, Albany

Fourth District Branch—**Richard A. Hughes, Sr., M.D.**, Warren

Fifth District Branch—**Richard J. Freeman, M.D.**, Cayuga

Sixth District Branch—**William A. Dolan, M.D.**, Monroe

Seventh District Branch—**Joyce M. McChesney, M.D.**, Monroe

Eighth District Branch—**Amy Early, M.D.**, Erie

Ninth District Branch—**Robert A. Mayers, M.D.**, Westchester

Member-at-Large—**William B. Rosenblatt, M.D.**, New York

Excused was: Jeffrey A. Ribner, M.D., Sixth District Branch. President Morton M. Kurtz, M.D., designated William A. Dolan, M.D., to represent the interest of the Sixth District Branch.

After careful consideration of the recommendations submitted by the district branches, county medical societies, and the resident, student and young physician sections in response to a memorandum, dated July 2, 1992, your Committee respectfully nominated the following candidates for election on March 14, 1993:

President—**Stanley A. Steckler, M.D.**, Suffolk

President-Elect—**James H. Cosgriff, Jr., M.D.**, Erie

Vice-President—**Stuart I. Orsher, M.D., J.D.**, New York

Secretary—**George Lim, M.D.**, Oneida

Assistant Secretary—**Joyce M. McChesney, M.D.**, Monroe

Treasurer—**Antonio F. LaSorte, M.D.**, Broome

Assistant Treasurer—**Stanley L. Grossman, M.D.**, Orange

Speaker—**Seymour R. Stall, M.D.**, Dutchess

Vice-Speaker—**John H. Carter, M.D.**, Albany

Councilors: (four for three years)—**Randall D. Bloomfield, M.D.**, Kings

—**Robert M. George, M.D.**, Oneida

—**David T. Hannan, M.D.**, Wayne

—**Samuel H. Madell, M.D.**, New York

Resident Councilor-(one for one year)—****Bryan Steinberg, M.D.**, New York

Student Councilor-(one for one year)—***Dawn Gangi, The Bronx**

Trustees: (two for five years)—**Charles N. Aswad, M.D.**, Broome

—**William A. Dolan, M.D.**, Monroe

Nomination for one-year term as AMA Student Alternate Delegate

(Term: January 1, 1994–December 31, 1994)—**Tanvir Choudhri, *** New York.

Nominations for AMA Delegates—(2 year terms—1/1/94 to 12/31/95) and

Nominations for AMA Medical Student Delegate* and Resident Physician Delegate**—(1 year terms—1/1/94 to 12/31/94).

Bruce H. Berlin, M.D., Suffolk

Robert Bonvino, M.D., Richmond

John H. Carter, M.D., Albany

Ann C. Cea, M.D., Westchester

****Larry Charlamb, M.D.**, Onondaga

Duncan W. Clark, M.D., Kings

James M. Flanagan, M.D., Wayne

Samuel M. Gelfand, M.D., Nassau

Robert M. George, M.D., Oneida

Morton M. Kurtz, M.D., Queens

Thomas A. Lansen, M.D., Westchester

Antonio F. LaSorte, M.D., Broome

George Lim, M.D., Oneida

David B. L. Meza, III, M.D., Orleans

Nancy H. Nielsen, M.D., Ph.D., Erie

Stuart I. Orsher, M.D., J.D., New York

John A. Ostuni, M.D., Nassau

Bernard J. Pisani, M.D., New York

Patricia A. Randall, M.D., Onondaga

Nathan P. Reed, M.D., Albany

Charles D. Sherman, Jr., M.D., Monroe

Seymour R. Stall, M.D., Dutchess

Edward C. Tanner, M.D., Monroe

***Edward Tuohy, New York**

The twelve nominees receiving the largest number of votes will be delegates; the second twelve will be alternates.

*Medical Student
**Resident Physician

Respectfully submitted,

Charles N. Aswad, M.D., *Chairman*

HOUSE COMMITTEE ON BYLAWS

To the House of Delegates, Ladies, and Gentlemen:

The members of the House Committee on Bylaws are as follows:

Stanley F. Brunn, M.D., Chairman Orange
Rodman D. Carter, M.D. Otsego
Louis W. Giordano, M.D. Broome
Robert M. Kohn, M.D. Erie
Thomas Lansen, M.D. Westchester
Sidney Mishkin, M.D. Nassau
Donna B. O'Hare, M.D. New York
Marilyn Pearl, M.D. New York
Hilda Ratner, M.D. Queens
Morton M. Kurtz, M.D. President, ex officio, Queens
George Lim, M.D. Secretary, ex officio, Oneida
Seymour Stall, M.D. Speaker, ex officio, Dutchess
Donald F. Foy Executive Vice-President, ex officio
William R. Egan Deputy Exec. Vice President, ex officio
Donald R. Moy, Esq. General Counsel, ex officio

A meeting of the Reference Committee on Bylaws was held at the Marriott Hotel in New York City on March 20, 1992. The Reference Committee prepared a transcript of testimony and submitted a summary of its recommendations to the House Committee on Bylaws. The input received from the meeting of the Reference Committee on Bylaws proved to be of great assistance to the House Committee on Bylaws when it met on November 16, 1992.

Three resolutions asking for amendments to the Bylaws were referred to the Committee for consideration.

Resolution 92-1, Reinstatement of Members Dropped for Nonpayment of Dues

Introduced by the New York County Medical Society

Whereas, Each year 400 to 550 physicians are dropped from the rolls of membership of the Medical Society of the State of New York for nonpayment of dues; and

Whereas, These numbers are growing; and

Whereas, In order to be reinstated as members such physicians must pay dues for the year in which membership was dropped in addition to the current year's dues; and

Whereas, This reinstatement penalty does not apply to those who resigned from membership, yet members may not be aware of the need to resign in order to be exempt from the reinstatement penalty; and

Whereas, This penalty discourages physicians from renewing membership; therefore be it

Resolved, That Article II, Section 2, paragraph 14 of the Bylaws of the Medical Society of the State of New York be amended to read as follows: (deletions lined through, additions underlined)

"Medical Society of the State of New York dues of a member reinstated after October 1 shall be credited to the succeeding year, all rights and privileges of membership, however, dating from the time of reinstatement; but no member dropped for nonpayment of dues and assessments shall be reinstated until he has, in addition, paid

his dues and assessments for the year in which he was dropped."

and be it further

Resolved, That Article II, Section 2, paragraph 15 be deleted. Paragraph 15 reads as follows: (deletions lined through)

~~"The provision in Article II, Section 2, paragraph 14 that no member dropped for nonpayment of dues and assessments shall be reinstated until he has, in addition, paid his dues and assessments for the year in which he was dropped, shall not be in effect for the period beginning June 6, 1985 through April 1, 1986."~~

and be it further

Resolved, That Article XV, paragraph 9, be amended to read as follows: (deletions lined through)

"Dues and State Society assessments of a member elected or reinstated after October 1 shall be credited to the succeeding year, but no member dropped for nonpayment of dues and assessments shall be reinstated until he has, in addition, paid his dues and assessments for the year in which he was dropped."

and be it further

Resolved, That Article XV, paragraph 10, be deleted. Paragraph 10 reads as follows: (deletions lined through)

~~"The provision in Article XV, paragraph 8 that no member dropped for nonpayment of dues and assessments shall be reinstated until he has, in addition, paid his dues and assessments for the year in which he was dropped, shall not be in effect for the period beginning June 6, 1985 through April 1, 1986."~~

The House Committee on Bylaws recommends that Resolution 92-1 be amended by the addition of the following:

Resolved, That Article II, Section 2 be amended by adding a new paragraph 15 to read as follows:

"Upon reinstatement to membership, the period of time in which membership had been dropped shall be considered a lapse in consecutive years of membership for the purpose of determining eligibility for life membership in accordance with Article II, Section 1, paragraph 6 of these Bylaws unless the reinstated member in addition pays the dues and assessments that accrued during the period in which membership had been dropped, in which case it shall be deemed that there was no lapse in consecutive years of membership for the purpose of determining eligibility for life membership."

and be it further,

Resolved, That Article XV be amended by adding a new paragraph 10 to read as follows:

"Upon reinstatement to membership, the period of time in which membership had been dropped shall be considered a lapse in consecutive years of membership for the purpose of determining eligibility for life membership in accordance with Article II, Section 1, paragraph 6 of these Bylaws unless the reinstated member in addition pays the dues and assessments that accrued during the period in which membership had been dropped, in which

case it shall be deemed that there was no lapse in consecutive years of membership for the purpose of determining eligibility for life membership."

The reinstatement penalty has seriously hampered the membership recruitment efforts of MSSNY and the county medical societies. Experience shows that when the reinstatement penalty was dropped during the period June 6, 1985 through April 1, 1986, MSSNY had its greatest success in having former members rejoin MSSNY and the county medical societies. The House Committee on Bylaws now believes that the reinstatement penalty relating to dues should be eliminated in order to maximize membership recruitment efforts.

Resolution 92-1 as amended would permit the reinstatement of members without the reinstatement penalty relating to dues, but will also provide an incentive to some reinstated members to pay, in addition, the dues and assessments that accrued during the period in which membership was dropped. By paying the past accrued dues and assessments, the reinstated member will be deemed not to have suffered a lapse in consecutive years of membership for purposes of determining eligibility requirements for life membership. This provision should be a strong incentive to rejoin particularly for those physicians who were members of MSSNY for many years and who recently dropped their membership.

Accordingly, the House Committee on Bylaws recommends that resolution 92-1 be **ADOPTED**, as amended.

Resolution 92-90, Expenses of Physicians Attending Young Physician Section Annual Assembly

Introduced by The Young Physician Section

Whereas, The purpose of the Young Physician Section (YPS) is to foster greater involvement by young physicians in the State and county medical societies; and

Whereas, The Young Physician Section budget for the first two years of the Section's existence provided travel costs for county delegates to attend the MSSNY YPS Annual Assembly; and

Whereas, These travel costs are to be assumed by county medical societies for 1993; and

Whereas, Many county medical societies might find it burdensome to assume these expenses, and the YPS meeting attendance might suffer as a result; and

Whereas, Precedent has been established to assist county medical societies with funds to cover the expenses of delegates to MSSNY's House of Delegates Meeting; therefore be it

Resolved, That Article XVI of the Bylaws of the Medical Society of the State of New York be amended by the addition of a new paragraph 6 to read as follows:

"Each component county medical society shall also be reimbursed by the Medical Society of the State of New York with an allowance of up to 50% of travel expenses, but not more than \$100 for one delegate to attend the Young Physician Section Annual Assembly."

and be it further;

Resolved, That, if adopted, this policy be effective for the 1993 Annual Assembly of the Young Physician Section.

FISCAL NOTE: \$5,500

The Committee submits the following substitute resolution for Resolution 92-90

Resolved, That Article XVI of the Bylaws of the Medical Society of the State of New York be amended by the addition of a new paragraph between paragraphs 5 and 6 to read as follows:

"Each component county medical society shall also be reimbursed by the Medical Society of the State of New York with an allowance of up to 50% of travel expenses, but not to exceed an amount to be set by the Board of Trustees each year for one delegate to attend the Young Physician Section Annual Assembly."

and be it further;

Resolved, That, if adopted, this policy be effective starting with the 1993 Annual Assembly of the Young Physician Section.

FISCAL NOTE: Approximately \$5,500

In order to foster greater involvement by young physicians in the State and county medical societies, it is critically important that the Young Physician Section be active and that the General Assembly of the Young Physician Section be well attended. Substitute Resolution 92-90, will provide necessary financial support to the YPS Annual Assembly, while preserving the authority of the Board of Trustees to determine the level of support in accordance with fiscal constraints.

Accordingly, the House Committee on Bylaws recommends that the proposed substitute resolution be **ADOPTED** in lieu of Resolution 92-90.

Resolution 92-97, Enrollment of New Physicians in County and State Medical Societies

Introduced by The Young Physician Section

Whereas, Young physicians are poorly represented at the county and state level; therefore be it

Resolved, That Article XV, paragraph 3 of the Bylaws of the Medical Society of the State of New York be amended to read as follows: (additions underlined, deletions lined through)

"The dues and assessments of those active members who have been graduated from medical or osteopathic college not more than five calendar years, not counting active service in the armed forces of the United States or in the United States Public Health Service, shall be one-third the amount levied on all other active members. The dues and assessments of those active members who have not completed their continuous residency training shall be one-tenth the amount levied on all other active members. In no case may an active physician continue to pay such reduced dues more than seven years after the date of graduation from medical or osteopathic school. The dues and assessments of all active members entering practice for the first time, ~~who are not otherwise eligible for reduced dues as set forth in prior provisions in this paragraph~~, shall be waived one half the amount levied on all other active members for the first two years of practice; full dues shall be paid after the

first two years of practice. Once an active member pays full dues, he shall no longer qualify for half-dues status."

All physicians, including young physicians, have a vital stake in the continuing ability of the Medical Society to represent the medical profession as a whole and to advocate health related rights, responsibilities and issues. If the viability of the Medical Society is to continue, it is important that all physicians having a stake in the Medical Society share in the responsibility of paying dues. The current provision in the Bylaws of the Medical Society providing one half dues and other levels of reduced dues are believed to be adequate and reasonable, but the outright waiver of dues for physi-

cians entering practice for the first time would be inappropriate.

Accordingly, the House Committee on Bylaws recommends that Resolution 92-97 **NOT BE ADOPTED**.

Your Chairman would like to thank, in addition to the members of the Committee and the physicians and other individuals who testified before it, those members of staff who helped this Committee: Donald R. Moy, Esq., Jay. B. Silverman, Esq. and Deborah Gerrity.

Respectfully submitted
Stanley F. Brunn, M.D., *Chairman*



Our Service Speaks for Itself

"Thanks for your prompt attention to my claim. Your service is most certainly the best." "I congratulate your agency on the handling of my recent claim...At no time was there any quibbling or any effort made to avoid the payments which were always made on time." "...deep gratitude for the way you helped us both during the trying times of the last three years." "Your readiness to advise and your human approach will not be forgotten." "Again, I wish to reiterate what I have said before, that service and **CHARLES J. SELLERS and COMPANY** are synonymous." "...All during this time the Charles J. Sellers Agency paid me very promptly and graciously." "...thank you for your unbelievably fast settlement of my claim..." "...it is a refreshing change to deal with an Agency that takes care of its clients."



CHARLES J. SELLERS & COMPANY INC.

4300 CAMP ROAD • PO BOX 460
ATHOL SPRINGS, NEW YORK 14010
TOLL FREE 1-800-333-5440



PHYSICIANS WANTED—CONT'D

HELP WANTED: Neurologist/Physiatrist for busy Western Nassau County Medical Center. Salary commensurate. Please call (516) 538-6535.

INTERNAL MEDICINE Attractive financial package, full range of benefits and MINIMAL on-call schedule. This is an opportunity to join an established HMO group in Rochester, New York. Rochester is a beautiful, exciting city with a low cost of living. If you are interested in providing primary care services in a contract management setting with no administrative hassles, submit CV to 2828 Croasdale Drive, Durham, NC 27705 or call 1-800-678-2811 for more information.

NORTHEAST—Established internal medicine solo practice, affiliated with JCAH accredited hospital. Brand new, 24 hour, staffed ER. Excellent hospital sponsored income guarantee, with potential for higher gross. Extensive benefits package. Located in four college community. Contact Darlene 1-800-669-9822.

NEW YORK—Four college community. Diversified recreational and cultural activities. JCAH accredited hospital seeks OB/GYN. Fetal monitoring equipment and sonogram. 1:3 coverage. Excellent income guarantee with potential to gross double within three years. Excellent benefits. Call Darlene 1-800-669-9822.

NEW YORK—Established solo practice affiliated with JCAH approved hospital in four college community seeks urologist. 15–25 patients/day, 4–7 procedures in OR/week, 50 TUR/year. Ultrasound unit and flow meter. Excellent income guarantee. Excellent benefits. Call Darlene 1-800-669-9822.

N.Y. DOCTORS FINED!

OSHA TARGETS REGION II

After employee complaints, citations are being issued against New York medical professionals. Protect yourself from employee lawsuits and OSHA fines.

- Easy to use training guidebook
- Step-by-step audio tape
- All necessary forms

Over 2000 programs sold at \$395
AMA Members' cost now only \$99⁰⁰



Federal Health and Safety Regulations, Simplified

1-800-456-8375

Ask for Laurie

IT'S A TRAGEDY BEYOND DESCRIPTION.



96,000 acres of irreplaceable rain forest are being burned every day.



These once lush forests are being cleared for grazing and farming. But the tragedy is without the forest this delicate land quickly turns barren.

In the smoldering ashes are the remains of what had taken thousands of years to create. The life-sustaining nutrients of the plants and living matter have been destroyed and the exposed soil quickly loses its fertility. Wind and rain reap further damage and in as few as five years a land that was teeming with life is turned into a wasteland.

The National Arbor Day Foundation, the world's largest tree-planting environmental organization, has launched Rain Forest Rescue. By joining the Foundation, you will help stop further burning. For the future of our planet, for hungry people everywhere, support Rain Forest Rescue. Call now.



 The National
Arbor Day Foundation

Call Rain Forest Rescue NOW.
1-800-255-5500

MEETINGS AND LECTURES

The New York State Journal of Medicine cannot guarantee publication of meeting and lecture notices. Information must be submitted at least three months prior to the event.

FEBRUARY 1993

AROUND THE STATE

BRONX

Feb 25-26. Practical Anatomy. 14.25 Cat I Credits. Albert Einstein College of Medicine, Bronx. Contact: June Lewis, Office of Continuing Medical Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

HUNTINGTON

Feb 2. Pediatric Headaches. Feb 9. Seizure Disorders. Feb 16. Early Childhood Development. Feb 23. Hypertension in Children. Schneider Children's Hospital at Huntington Hospital Grand Rounds. Contact: Arthur J. Schwager, MD, 164 E Main Street, Huntington, NY 11743. Tel: (516) 427-0530.

MANHATTAN

Feb 17. ENT for the Internist. Update Asthma. Cornell University Medical College Uris Auditorium. Contact: Association of Practicing Physicians, Cornell University Medical College, 445 E 69th St, New York, NY 10021. Tel: (212) 746-4752.

Feb 26-28. NYU/Bellevue Hospital Center Psychiatry Board Review. 24.5 Cat I Credits. NYU Medical Center. Contact: NYU Medical Center, 550 Fifth Avenue, New York, NY 10016. Tel: (212) 263-5295.

AROUND THE NATION

ARIZONA

Feb 15-19. Psychopharmacology Review Course. Westin LaPaloma Resort, Tucson. **Feb 19-20. Geriatric Rheumatology & Rehabilitation.** Radisson Hotel, Tucson. **Feb 22-25. Post Graduate Course Practical Radiology.** Loews Ventana Canyon Resort, Tucson. Contact: Continuing Medical Education, Arizona Health Sciences Center, Tucson, AZ 85724. Tel: (602) 626-7832.

CALIFORNIA

Feb 4-6. 11th Annual Practical Update of Infectious Disease. 12 Cat I Credits. Hilton Hotel, Sacramento. Contact: Office of Continuing Medical Education, UC Davis Medical Center, 2701 Stockton Blvd, Sacramento, CA 95817. Tel: (916) 734-5390.

Feb 11-13. Recent Advances in Neurology. Ritz-Carlton Hotel, San Francisco. Contact: Extended Programs in Medical Education, Room LS-105, University of California, San Francisco, CA 94143. Tel: (415) 476-4251.

Feb 18-21. 14th Annual Meeting of the American Society of Outpatient Surgeons. Hyatt Islandia Hotel, San Diego. Contact: the American Society of Outpatient Surgeons, 4805 Mercury St, Suite E, San Diego, CA 92111-2110. Tel: (619) 279-1325.

DISTRICT OF COLUMBIA

Feb 8-10. Obstetric Controversies. Feb 11-13. Common Gynecologic Problems. Feb 25-27. Gynecologic Surgery. ACOG Freestanding Postgraduate Courses. 16 Cognates. Contact: Mary Givens, Registrar, The American College of Obstetricians and Gynecologists, 409 12th St SW, Washington, DC 20024-2188. Tel: (800) 673-8444 ext 2541.

FLORIDA

Feb 8-10. State of the Art OB/GYN. 11 Cat I Credits. Good Samaritan Medical Center, West Palm Beach. Contact: Laura J. Keech, CME Coordinator, Good Samaritan Medical Center, PO Box 3166, West Palm Beach, FL 33402-3166. Tel: (407) 650-6236.

Feb 8-12. Controversies and Recent Advances in Surgical Pathology. Disney Contemporary Hotel, Buena Vista. Contact: Center for Advanced Medical Education, Armed Forces Institute of Pathology, Washington, DC 20306-6000. Tel: (301) 427-5001.

Feb 15-19. Diagnostic Imaging Update: Mammography, MRI, Body Imaging, Neuroradiology, Pediatrics. 23.75 Cat I Credits. The Ritz-Carlton Hotel, Palm Beach. **Feb 22-26. Magnetic Resonance Imaging.** 21 Cat I Credits. The Ritz-Carlton Hotel, Naples. Contact: Dawne

(continued on p 11A)

(continued from p 10A)

Ryals, Ryals and Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: (404) 641-9773.

HAWAII

Feb 22-26. Diagnostic Imaging Update. The Ritz-Carlton Resort Hotel, Maui. Contact: Dawne Ryals, Ryals and Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: (404) 641-9773.

NEW JERSEY

Feb 18-19. Quality Management for the Medical and Dental Professional. Princeton. Contact: Philip Crosby Associates. Tel: (800) 722-1464.

PUERTO RICO

Feb 8-12. Current Topics in Diagnostic Imaging. 22.5 Cat I Credits. Hyatt Regency, Cerramar Beach. Contact: NYU Medical Center Post-Graduate Medical School, 550 Fifth Avenue, New York, NY 10016. Tel: (212) 263-5295.

UTAH

Feb 6-13. 10th Annual Office Based Sports Medicine. 26 Cat I Credits. Shadow Ridge Resort Hotel, Park City. Contact: Extended Programs in Medical Education, Registration Office, Room LS-105, University of California, San Francisco, CA 94143-0742. Tel: (415) 476-4251.

VERMONT

Feb 9-12. Ninth Annual Clinical Update in OB/GYN. 12 Cat I Credits. Stratton. Contact: Office of Continuing Medical Education, Albany Medical College, 47 New Scotland Ave, Albany, NY 12208. Tel: (518) 445-5828.

WASHINGTON

Feb 27. Malpractice. Washington University Medical Center. Contact: Washington University School of Medicine, CME, Campus Box 8063, 660 South Euclid Ave, St Louis, MO 63110-1093. Tel: (800) 325-9862.

AROUND THE WORLD

MEXICO

Feb 14-21. Pediatric Update 1993. 22.75 Cat I Credits. Acapulco. Contact: June Lewis, Office of Continuing Medical Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650. □

YOCON®

YOHIMBINE HCl

Description: Yohimbine is a 3a-15a-20B-17a-hydroxy Yohimbine-16a-carboxylic acid methyl ester. The alkaloid is found in Rubaceae and related trees. Also in Rauwolfia Serpentina (L) Benth. Yohimbine is an indolalkylamine alkaloid with chemical similarity to reserpine. It is a crystalline powder, odorless. Each compressed tablet contains (1/12 gr.) 5.4 mg of Yohimbine Hydrochloride.

Action: Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it; however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

Indications: Yocon® is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

Contraindications: Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.^{1,2} Also dizziness, headache, skin flushing reported when used orally.^{1,3}

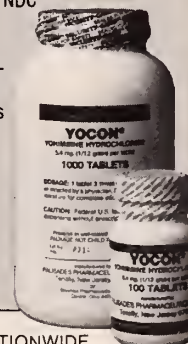
Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

How Supplied: Oral tablets of Yocon® 1/12 gr. 5.4 mg in bottles of 100's NDC 53159-001-01 and 1000's NDC 53159-001-10.

References:

1. A. Morales et al., New England Journal of Medicine: 1221, November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

Rev. 1/85



AVAILABLE AT PHARMACIES NATIONWIDE

**PALISADES
PHARMACEUTICALS, INC.**

219 County Road
Tenafly, New Jersey 07670
(201) 569-8502
1-800-237-9083

PRACTICES AVAILABLE

OB-GYN PRACTICE FOR SALE: Excellent opportunity for physician to purchase an established OB-GYN practice. Prime location in Maplewood, NJ. High yearly gross income. Will introduce. Terms available. Call Michael Wiley at (516) 665-0439.

INTERNAL MEDICINE PRACTICE FOR SALE: Excellent opportunity for physician to purchase an established Internal Medicine practice. Prime location in West Islip, Long Island, New York. Excellent yearly gross income for 30 hours per week. Excellent growth potential. Will introduce. Terms available. Call Michael J. Wiley at (516) 665-0439.

PRACTICES WANTED

M.D. SEEKS TO RELOCATE his 40 years of expertise in General and Comprehensive Medicine (plus specialty qualifications). Prefers area where good outpatient care is appreciated. Can expand existing practice or start new one. Reply Dept. 514 c/o NYSJM.

EQUIPMENT

OUR ABODIA SLIDE STORAGE SYSTEM holds 1,000 to 12,000 slides. View 100 to 200 slides at once. Any slide collection becomes manageable. Find, select, sort slides—quickly and conveniently. Individual slides and entire racks are removable. Slide presentations & lectures are easy to assemble, and quick to sequence. For catalog call (800) 950-7775 or FAX (304) 344-4764.

REAL ESTATE FOR SALE OR RENT

MANHATTAN'S UPPER EAST SIDE. 133 EAST 73 STREET. Lexington Professional Center. Hourly, part-time or full-time medical and psychiatric suites. Fully furnished and equipped. 24-hours answering service, receptionist, and mail service. Clinical laboratory on premises. No leases required, no minimum hours required. (212) 861-9000.

FOR SALE: EAST SIXTIES, PROFESSIONAL BUILDING. Large medical office (2,250 sq. ft.). 3 consultation rooms, 4 treatment rooms, laboratory, 2 bathrooms, large reception area. Also suitable for dentist. Full-time doorman. Call (212) 838-2860.

SHARE OFFICE FOREST HILLS, Queens Blvd. Fully furnished and equipped. Ideal specialist. Near all transportation. One to three days a week. Immediate. Dr. Sharon (718) 793-6832.

MANHASSET-HOME/MEDICAL OFFICE FOR SALE. Adjacent to St. Francis Hospital. 4½ Room Office. 7 Room Residence. High \$500's. Phone 516-627-2234.

PHYSICIANS: NO INVESTMENT TO OPEN YOUR OWN PRACTICE! Great opportunity in beautiful, fully equipped office suite on Long Island's North shore. Includes state-of-the-art equipment, efficient administrative and medical support staff, on-site lab. Ideal for cardiologist, allergist, endocrinologist, etc. P/T or F/T basis. Call Gloria. 516-496-7585.

MISCELLANEOUS

PROFESSIONAL CONDUCT EXPERT. Robert S. Asher, J.D., M.P.A., in health, former Director Professional Conduct, N.Y.S. Board of Regents, now in private legal practice. 15 years health law experience concentrating on professional practice, representation before government agencies on Disciplinary, Licensure, Narcotic Control, Medicaid, Medicare of Third-Party Reimbursement matters and professional business practice. Robert S. Asher, Esq., 295 Madison Ave., Suite 700, NYC. (212) 697-2950 or evenings (914) 723-0799.

SONOGRAMS—Cardiac echo, osteoporosis bone densitometry. In your office or patient's home. Legally proper rent arrangements. 718-367-7667.

SHAPIRO & BYRNE, P.C., ATTORNEYS AT LAW. Daniel M. Shapiro, M.D., J.D. Professional misconduct representation including disciplinary proceedings, medical staff problems and hospital privileges, peer review proceedings and other matters affecting the professional life of physicians. 220 Old Country Road, Mineola, N.Y. (212) 514-5755, (516) 877-1055.

PROFESSIONAL MISCONDUCT ADVOCACY with dignity and concern. George Weinbaum, Esq., former deputy director of the New York State Attorney General's office for Medicaid Fraud Control and also former Director of Medicare and private insurance investigations for Empire Blue Cross/Blue Shield. Extensive experience and attention is devoted to Misconduct Avoidance, Disciplinary Proceedings, Medicaid/Medicare issues, Controlled Drug Proceedings, Audits, and Federal/State civil and criminal investigations. Consultations available. George Weinbaum, Esq., 3 Barker Avenue, White Plains, New York 10601. Telephone (914) 686-9310—24 hours.

LIFSHUTZ, POLLAND & ASSOCIATES, P.C. The law firm that specializes in health care representation. Our experienced staff of attorneys have successfully represented physicians and other health care professionals in such matters as managed care ventures and contracts, establishment of medical groups, counseling professional societies and hospital medical staffs, hospital privileges, defense of Medicaid/Medicare abuse allegations (civil and criminal), third-party beneficiary termination, peer review, challenging legislative and regulatory enactments, leasing and subleasing of medical office space, tax and pension plan structuring of professional corporations, estate planning, litigation of rights and interests of clients including equitable distribution of physician's licenses in matrimonial actions. Lifshutz, Polland & Associates, P.C., Attorneys at Law, 675 Third Avenue, New York, N.Y. 10017. (212) 949-8484.

MEDICAL COLLECTION AGENCY—Specializing in medical collections only! We offer conscientious attention to your unpaid bills in an appropriate and courteous manner. Your past due office accounts are collected for a 30% fee. For further information please call: (516) 475-1092, and ask for Janet. M.C.A., L.P., 250 Yaphank Road, East Patchogue, NY, 11772.

MISCELLANEOUS—CONT'D

IS ACTION BEING TAKEN AGAINST YOUR LICENSE TO PRACTICE MEDICINE? If affirmative, contact Susan Kaplan, Attorney-at-Law, (212) 877-5998. Practice limited to assisting, advising and defending physicians in professional misconduct (licensure) proceedings before the Office of Professional Medical Conduct, issues relating to chemical dependence and restoration of medical licenses—with extensive trial and administrative experience—formerly Assistant Chief of Prosecution and Deputy Director of Prosecution for New York State's Office of Professional Discipline (the state agency responsible for regulating NYS's 31 licensed professions), and as an Assistant District Attorney in Nassau County.

MEDICAL TRANSCRIPTION—Nassau County. 25 Years' experience. Thorough knowledge of all medical specialties. IBM Wordprocessing, Microbank-25, Modem transmittal available. Phone in dictation. Patient chart notes, in-office tests, consultation letters. Call Wordbusters (516) 333-8660.

WOOD & SCHER, ATTORNEYS AT LAW. Former Chief Enforcement Officers for the Office of Professional Discipline, now representing licensed professionals in matters of: Professional misconduct proceedings, License application/restoration, Controlled Drug Proceedings, Medicaid/Medicare Proceedings, Hospital Privileges, Malpractice Defense. Call for a consultation William L. Wood, Jr. and Anthony Z. Scher, (914) SCarsdale 3-3500.

PHYSICIANS SIGNATURE LOANS TO \$50,000. Take up to 7 years to repay with no pre-payment penalties. Competitive fixed rate. Use for taxes, investment consolidation or any other purpose. Prompt, courteous service. Physicians Service Association, Atlanta, GA. Serving MD's for over 10 years. Toll-free (800) 241-6905.

WANT DISCOUNTS ON YOUR EXISTING INSURANCE? We provide complimentary 2nd opinions on your disability and life insurance to provide you with the lowest rates. Servicing physicians exclusively. References provided upon request. Paul R. Sheinkopf, Sheinkopf & Associates, EAB Plaza West, 5th floor, Uniondale, NY 11556-0137. 516-357-8700 FAX 516-357-8891.

HIGH QUALITY TRANSCRIPTION at an affordable price. All specialties. Also medicolegal transcription, journal articles, manuscripts and book chapters expertly done. Audiocassettes, on-line phone dictation 24-hours per day 7 days per week. Competitive prices. Call 718-225-0806.

TRIAL ATTORNEY. Kenneth I. Wirfel, Esq. former Federal Prosecutor and Adjunct Associate Professor Trial Advocacy, NY Law School, with expertise in representing licensed professionals in connection with allegations of Medicaid/Medicare fraud; Grand Jury investigations, criminal prosecutions and parallel administrative proceedings. All Federal and State Courts. Kenneth I. Wirfel, Dienst & Serrins, 225 Broadway, New York, NY 10007. (212) 406-1700.

REPRESENTATION OF PHYSICIANS and advice and counsel with respect to licensure and professional conduct matters, audit preparations, reimbursement issues and governmental inquiries and investigations. David E. Ruck, Esq., former Chief, Criminal Division, Office of the New York State Special Prosecutor for Medicaid Fraud Control. Mr. Ruck's law offices: 230 Park Avenue, Suite 2830, New York, New York 10169. Telephone 212-661-8070.

Classified Advertising

New York State Journal of Medicine

GENERAL INFORMATION

All classified advertisements are payable in advance, except for government agencies and advertising agencies; a 15% commission to recognized advertising agencies.

Frequency: Monthly

Mailing date: 7th of the month

Closing date: 30 days before mailing date

Circulation: 28,000 (mainly physicians & medical libraries)

DISPLAY ADVERTISING

	<i>1 time</i>	<i>6 time</i>	<i>12 time</i>	<i>Width</i>	<i>Depth</i>
1/4-page	\$750	\$695	\$635	3-1/2" ×	4-7/8"
1/6-page	365	340	315	2-1/8" ×	4-7/8"
1/8-page	340	315	290	3-1/2" ×	2-3/8"
1/16-page	215	200	185	3-1/2" ×	1-1/8"
1/18-page	185	170	155	2-1/8" ×	1-1/2"

PARAGRAPH ADVERTISING

The first several words are set in bold face caps.

Rates: \$55.00 per insertion for 50 words or less; additional words are 60 cents each. On request, Dept. numbers will be assigned by the Journal for replies to be forwarded to the advertiser. Dept. numbers are \$1.00 per insertion. There is no frequency discount for paragraph ads.

Counting Words: Two initials, each abbreviation, figures consisting of 5 numerals or less, are counted as separate words. For replies, your name and address, or telephone number should appear at the end of the ad and be counted in the total number of words.

For further information, please call the Advertising Department at 516-488-6100.

CLASSIFIED ADVERTISING ORDER FORM

New York State Journal of Medicine
Attn: Classified Advertising
P.O. Box 5404
Lake Success, N.Y. 11042-5404

Date_____

Name_____

Payment enclosed: \$_____

Address_____

Number of Insertions: _____

City/State/Zip_____

Assign Dept. Number: _____

Please make check payable to New York State Journal of Medicine.



The Gift of Life

The children at St. Jude Children's Research Hospital take life one day at a time. At St. Jude, every second counts. The children here are fighting for their lives.

The doctors and researchers at St. Jude are working to find a way to defeat the deadly enemy: childhood cancer. Since St. Jude Hospital opened in 1962, it has forged new treatments for childhood cancer and has helped save the lives of thousands of children around the world. But the battle has just begun.

You can join the fight. To find out how, write to St. Jude Children's Research Hospital, P.O. Box 3704, Memphis, TN 38103. Or call 1-800-877-5833.



**ST. JUDE CHILDREN'S
RESEARCH HOSPITAL**

Danny Thomas, Founder



Doctor . .

Do you, or a physician you know, have a problem with alcohol, drugs, or emotional illness?

If so, please contact the Medical Society of the State of New York's Committee for Physicians' Health, whose function is to assist, *confidentially*.

Telephone: 800-338-1833.

Index to Advertisers

Bristol Myers	3rd & 4th Cover
Classified	8A, 9A, 12A
CompHealth	8A
Knoll Pharmaceuticals	1A, 2A
Eli Lilly and Company	7A
MLMIC	2nd Cover
Palisades Pharmaceuticals	11A
P.P.I.	9A
Charles J. Seller & Company, Ltd.	9A
U.S. Air Force	8A

PRAVACHOL® (Pravastatin Sodium Tablets)

CONTRAINDICATIONS

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

Pregnancy and lactation. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of child-bearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

WARNINGS

Liver Enzymes: HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin, the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

PRECAUTIONS

General: Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

Homozygous Familial Hypercholesterolemia. Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

Renal Insufficiency: A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 α -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t_{1/2}) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

Information for Patients: Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

Drug Interactions: Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS: Skeletal Muscle.

Antipyrine: Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

Cholestyramine/Colestipol: Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

Warfarin: In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C_{max} of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

Cimetidine: The AUC_{0-12h} for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

Digoxin: In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin and its metabolites (SQ 31,906 and SQ 31,945) was not affected.

Gemfibrozil: In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C_{max}, and T_{max} for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids (1 hour prior to PRAVACHOL), cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL (pravastatin sodium) was administered.

Other Drugs: During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

Endocrine Function: HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a $\geq 50\%$ rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

CNS Toxicity: CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallenian degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallenian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg/day dose.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year study in rats led pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose males than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK +/– mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

Pregnancy: Pregnancy Category X: See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg/day or in rabbits at doses of up to 50 mg/kg/day. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter²). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL (pravastatin sodium), it should be discontinued and the patient advised again as to the potential hazards to the fetus.

Nursing Mothers: A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

Pediatric Use: Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

ADVERSE REACTIONS

Pravastatin is generally well tolerated, adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

Adverse Clinical Events: All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below, also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug.

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N=900)	Placebo (N=411)	Pravastatin (N=900)	Placebo (N=411)
Cardiovascular				
Cardiac: Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8*	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

Skeletal: myopathy, rhabdomyolysis.

Neurological: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthena, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

Gastrointestinal: pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

Reproductive: gynecostasia, loss of libido, erectile dysfunction.

Eye: progression of cataracts (lens opacities), ophthalmoplegia.

Laboratory Test Abnormalities: Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

Concomitant Therapy: Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

OVERDOSAGE

There have been no reports of overdoses with pravastatin.

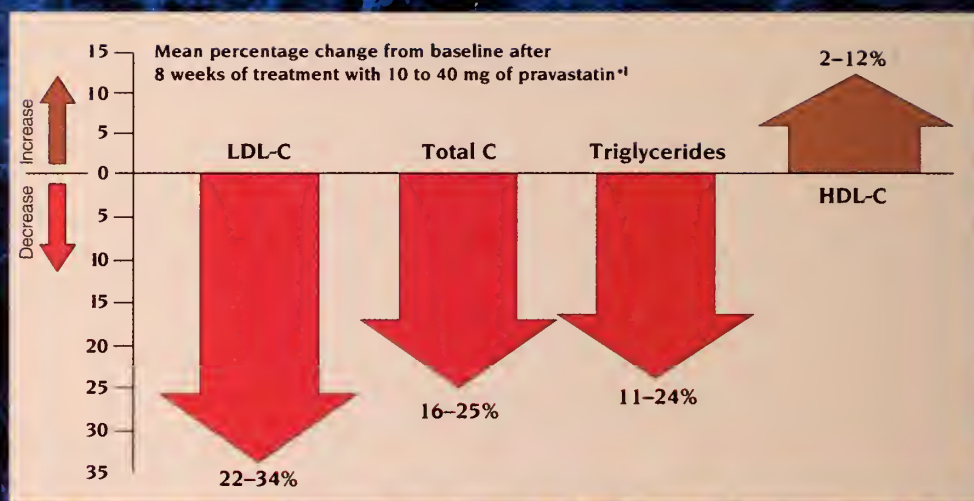
Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.





Effective cholesterol control

Consistently and significantly reduces total C and
atherogenic LDL-C; positively affects other key lipids



^aEach arrow represents a range of means derived from a single placebo-controlled study that included 55 patients treated with pravastatin.

PRAVACHOL[®] (pravastatin sodium) is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate.

Active liver disease or unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin.

Reference: 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study *Clin Cardiol*. 1991;14:146-151.

PRAVACHOL[™]
pravastatin sodium 20 mg tablets

Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



Bristol-Myers Squibb Company

New York State Journal of Medicine



VOL 93
NO 2
FEBRUARY
1993

HEALTH FRAUD

**WOLVES IN SHEEP'S
CLOTHING**

**COMBATting MEDICAL
FRAUD**

**AIDS FRAUD, FINANCES, AND
FRINGES**

**RECOGNIZING DECEPTION IN
THE PROMOTION OF
UNTESTED AND UNPROVEN
MEDICAL TREATMENTS**

**ALLERGY-RELATED
QUACKERY**

**THE PHYSICIAN'S ROLE IN
PROMOTING THE
SCIENTIFIC TREATMENT OF
CANCER AND
DISCOURAGING
QUESTIONABLE TREATMENT
METHODS**

**FERTILE FIELD FOR FADS
AND FRAUD:
QUESTIONABLE
NUTRITIONAL THERAPIES**

**PHYSICIANS IN DENTAL
QUACKERY**



Because One Size Doesn't Fit All...

New Humulin 50/50 is the tailor-made answer to individual patient needs. A unique combination of equal amounts of Regular human insulin and NPH human insulin, it will be useful in situations in which a greater initial insulin response is desirable for greater glycemic control.

Like Humulin 70/30*, new Humulin 50/50 offers the convenience and accuracy of a premix. And it can be used in conjunction with an existing 70/30 regimen.



New **Humulin** ⁵⁰/₅₀

50% human insulin
isophane suspension
50% human insulin injection
(recombinant DNA origin)

The Newest Option in Insulin Therapy

WARNING: Any change of insulin should be made cautiously and only under medical supervision.

* Humulin® 70/30 (70% human insulin isophane suspension, 30% human insulin injection [recombinant DNA origin]).



Global Excellence in Diabetes Care
Eli Lilly and Company
Indianapolis, Indiana
46285

PROTECTING YOUR PRACTICE IS A SIMPLE PROCEDURE WHEN YOU USE THE RIGHT INSTRUMENT.



Outstanding professional liability coverage and superior service are just a phone call away—with HUM.

To make your practice as safe as it can be, you need more than just insurance. You need a well-managed program to reduce risk. Education to keep current on important issues. Consultants to suggest alternatives—and work *with* you to implement them. You need to connect with HUM.

Every policy is based on partnership.

When HUM writes you a policy, we make a real commitment to serving you—from designing cost-effective coverage, to enhancing your risk management efforts, to managing claims prudently and professionally.

Along with unmatched financial strength, we offer competitive premiums, discounts for first-year and part-time practitioners, plus a range of flexible payment plans.

Best of all, it's simple to put our advantages into practice. Just dial 1-800-435-3558 for more information about HUM's policies.

We're on call for physicians.

A policy of partnership.



Hospital Underwriters Mutual
Insurance Company

8 British American Boulevard, Latham, NY 12110

New York State Journal of Medicine



COMMITTEE ON PUBLICATIONS, LIBRARY, AND ARCHIVES

MILTON GORDON, MD, Chairman

PHILIP P. BONANNI, MD, Vice-Chairman

JOSEPH I. COHN, MD

SHARON C. HERMAN MEAD, MD

JONATHAN A. HYDE (*Medical student*)

JOSEPH F. MURATORE, MD

STANLEY LUFTSCHEIN, MD

DONNA B. O'HARE, MD

JOHN T. PRIOR, MD

Editor PASCAL JAMES IMPERATO, MD

Consulting Editor JOHN T. FLYNN, MD

Consulting and Book

Review Editor RICHARD B. BIRRER, MD

Consulting Editor NAOMI R. BLUESTONE, MD, MPH

Consulting Editor CARL POCHEDLY, MD

Consultant in Biostatistics JOSEPH G. FELDMAN, DRPH

Managing Editor RALPH W. BATTEY

Advertising Production Coordinator KEVIN DAVEY

Copy Editor VICKI GLASER

Editorial Assistant MARYANN VIGLIOTTI

Administrative Assistant MAUREEN MAHER

Librarian ELLA ABNEY

ASSOCIATE EDITORIAL BOARD 1993

RANDALL BLOOMFIELD, MD

FLORENCE KAVALER, MD

ROBERT D. BRANDSTETTER, MD

JAMES M. MORRISSEY, ESQ

JOHN S. DAVIS, MD

STEPHEN NORDLICHT, MD

CHARLES D. GERSON, MD

JOSEPH SCHLUGER, MD

MYLES S. GOMBERT, MD

RICHARD A. STEIN, MD

ALFRED P. INGEGNO, MD

RODRIGO E. URIZAR, MD

ARTHUR H. WOLINTZ, MD

Microform copies. This publication is available on microform film. Address orders to University Microfilms, 300 North Zeeb Road, Ann Arbor, MI 48106.

Advertising representatives. *Pharmaceutical Advertising:* Cunningham Associates, PO Box 308, Park Ridge, NJ 07656. Telephone: (201) 767-4170. *Non-Pharmaceutical Advertising:* Cookson Media Services, Inc., PO Box 3669, Trenton, NJ 08629. Telephone: (609) 393-7196.

MEDICAL SOCIETY OF THE STATE OF NEW YORK

MORTON M. KURTZ, MD, *President*

STANLEY A. STECKLER, MD, *President-Elect*

CHARLES N. ASWAD, MD, *Past-President*

JAMES H. COSGRIFF, JR, MD, *Vice-President*

GEORGE LIM, MD, *Secretary*

JOYCE M. MCCHESENEY, MD, *Assistant Secretary*

ANTONIO F. LASORTE, MD, *Treasurer*

STANLEY L. GROSSMAN, MD, *Assistant Treasurer*

SEYMOUR R. STALL, MD, *Speaker*

JOHN H. CARTER, MD, *Vice-Speaker*

Councilors

Term Expires 1993

RANDALL D. BLOOMFIELD, MD, Kings
WILLIAM A. DOLAN, MD, Monroe
ROBERT M. GEORGE, MD, Oneida
STUART I. ORSHER, MD, New York

Term Expires 1994

ROBERT BRUCE BERGMANN, MD, Nassau
RICHARD A. HUGHES, MD, Warren
JEFFREY A. RIBNER, MD, Broome
ANTHONY P. SANTOMAURO, MD, Erie

Term Expires 1995

BRUCE H. BERLIN, MD, Suffolk
ALBERT M. ELLMAN, MD, Albany
FRED N. FLATAU, MD, Queens
SANFORD A. KAPLAN, MD, Westchester

Resident Councilor (representing the Resident Physician Section)

PAUL PIPIA, MD, New York

Student Councilor (representing the Medical Student Section)

LEON HENDERSON, New York

Trustees

JAMES M. FLANAGAN, MD, Wayne
(*Chairman*)

JOHN A. FINKBEINER, MD, New York

SAMUEL M. GELFAND, MD, Nassau

M. THEODORE TANENHAUS, MD, Kings

CHARLES D. SHERMAN, JR, MD, Monroe

DUANE M. CADY, MD, Onondaga

ROBERT A. MAYERS, MD, Westchester

Executive Vice-President

Deputy Executive Vice-President

Executive Vice-President Emeritus

Program Director, Committee for

Physicians' Health

Director, Division of Communications

Director, Division of Finance and

Administration

General Counsel

Director, Division of Governmental Affairs

Director, Division of

Management Information Services

Director, Division of Marketing and

Meeting Services

Director, Division of Membership

Support Services

Director, Division of Planning, Research, and

Development

Director, Division of Policy Coordination

Director, Division of Public Health and

Education

Director, Division of Scientific Publications

Director, Division of Socio-Medical

Economics

Consultant

DONALD F. FOY

WILLIAM R. EGAN

GEORGE J. LAWRENCE, JR, MD

LINDA A. LAMBERT

THOMAS M. DONOGHUE

PHILIP A. SCHUH, CPA

DONALD R. MOY, ESQ

GERARD L. CONWAY, ESQ

GEORGE J. ADJAMI

GERALD SULLIVAN

EUNICE M. SKELLY

MICHAEL W. DELANEY, CAE

IRMA A. ERICKSON

PETER B. FARNSWORTH, MD

PASCAL JAMES IMPERATO, MD

MARIO V. MENGHINI

EDWARD SIEGEL, MD

The New York State Journal of Medicine (ISSN 0028-7628) is published monthly by the Medical Society of the State of New York. Copyright © 1993, Medical Society of the State of New York. Material may be photocopied for noncommercial scientific or educational use only. Special arrangements and permission are required from the author(s) of the particular article and from the editor for any other purpose. The editors of the *Journal* assume no responsibility for opinions and claims expressed in the articles contributed by individual authors.

SUBSCRIPTION INFORMATION. The annual subscription for members (\$30.00) is included in the annual membership dues. The subscription rate to nonmembers in the United States and Canada is \$40.00 (\$45.00 for all other countries). The single copy rate is \$6.00 Domestic/Canada, and \$7.00 Foreign, except for special issues. This includes postage. Change of address requests should give both the old and new address and allow six weeks for changeover.

The address for EDITORIAL, CIRCULATION, and ADVERTISING OFFICES is PO Box 5404, Lake Success, New York 11042. Telephone: (516) 488-6100.

POSTAGE. Second class postage is paid at New Hyde Park, New York, and additional mailing office. POSTMASTER: Send POD Form 3579 to New York State Journal of Medicine, PO Box 5404, Lake Success, New York 11042.

HEADACHE

IN THE DECADE OF THE BRAIN

SATURDAY, MARCH 27, 1993, 8:15 A.M. TO 3:15 P.M.

THE EIGHTH HEADACHE SYMPOSIUM PRESENTED BY THE COMPREHENSIVE HEADACHE CENTER
AT THE GERMANTOWN HOSPITAL AND MEDICAL CENTER AND *TEMPLE UNIVERSITY SCHOOL OF MEDICINE

- **Migraine Diagnosis and Clinical Symptomatology**
Seymour Solomon, M.D.
Montefiore Medical Center

- **Migraine. Comorbid Psychological Conditions: Anxiety and Depression**
Kathleen Merikangas, Ph.D.
Yale University

- **Migraine Treatment: The British Perspective**
Marcia Wilkinson, M.A., D.M., F.R.C.P.
City of London Migraine Clinic

- **Tension-Type and Chronic Daily Headache**
Stephen D. Silberstein, M.D.
The Germantown Hospital and Medical Center

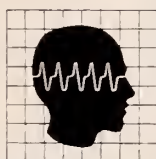
Register before March 6, 1993 by calling (215) 951-8926.
A \$25 registration fee is required made payable to The Germantown Hospital and Medical Center.



*Temple University School of Medicine is accredited by the Accreditation Council for Continuing Medical Education (AACE) to sponsor Continuing Education for physicians.

Temple University School of Medicine designates this CME activity for 6 credit hours in Category 1 of the Physicians' Recognition Award of the A.M.A.

Symposium funding provided by Glaxo, Inc. and Sandoz Pharmaceuticals. Additional funding by Abbott Laboratories and Carnrick Laboratories, Inc.



**COMPREHENSIVE
HEADACHE CENTER**

The Germantown Hospital and Medical Center
One Penn Boulevard • Philadelphia, PA 19144 • (215) 951-8926

MEETINGS AND LECTURES

The New York State Journal of Medicine cannot guarantee publication of meeting and lecture notices. Information must be submitted at least three months prior to the event.

MARCH 1993

AROUND THE STATE

GARDEN CITY

Mar 10. A Clinical Day in Ophthalmology Cornea. 7 Cat I Credits. Garden City Hotel. Contact: June Lewis, Office of Continuing Medical Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

HUNTINGTON

Mar 23. Assessment and Management of Shock in Pediatrics. 8:30 AM-9:30 AM at Huntington Hospital. Cat I Credits. Contact: Arthur J. Schwager, MD, Director, Continuing Pediatric Medical Educa-

tion, Huntington Hospital, Huntington, NY 11743. Tel: (516) 427-0530.

MANHATTAN

Mar 12-14. Interventional Laparoscopy and Stapling Techniques in Urology. 21.75 Cat I Credits. Grace Hall, Cabrini Medical Center. **Mar 15-19. Seminar in Advanced Rheumatology.** 25.5 Cat I Credits. **Mar 28-Apr 2. Anesthesiology Comprehensive Review XIII.** 45.5 Cat I Credits. NYU Medical Center. Contact: New York University, 550 First Ave, New York, NY 10016. Tel: (212) 263-5295.

Mar 18-20. 20th Annual Conference on Dyslexia. Sheraton Hotel. Contact: NY Branch, Orton Dyslexia Society, 71 W 23rd St, New York, NY 10010. Tel: (212) 691-1930.

Mar 18-19. Pain in Cancer and Aids. Waldorf Astoria Hotel. Contact: June Lewis, Office of Continuing Medical Education, Long Island Jewish Medical Center, New Hyde Park, NY 11042. Tel: (718) 470-8650.

Mar 24. Psycho-Pharmacology for the internist. Liaison Psychiatry. Cornell University Medical College, Uris Auditorium. Contact: Update Your Medicine, 445 E 69th St, Olin 328, New York, NY 10021. Tel: (212) 746-4752.

AROUND THE NATION

ARIZONA

Mar 6. Annual Epilepsy Update. Westin La Paloma Resort, Tucson. **Mar 12. Geriatric Medicine Update: Mental Health in the Elderly.** Doubletree Hotel, Tucson. **Mar 18-20. Symposium on Low Back Pain.** Loews Ventana Canyon Resort, Tucson. **Mar 22-26. Primary Care Update.** Westward Look Resort, Tucson. Contact: The University of Arizona Health Sciences Center, Office of Continuing Medical Education, Tucson, AZ 85724. Tel: (602) 626-7832.

CALIFORNIA

Mar 5. 19th Annual Diabetes Symposium. 6 Cat I Credits. Sheraton Hotel, Sacramento. Contact: UC Davis School
(continued on p 5A)

New York State Journal of Medicine

FEBRUARY 1993 / Volume 93, Number 2



Contents

COMMENTARIES

- 85 **Wolves in sheep's clothing**
RICHARD H. LANGE, MD
- 86 **Combatting medical fraud**
JANE E. HENNEY, MD

REVIEW ARTICLES

- 88 **Recognizing deception in the promotion of untested and unproven medical treatments**
GRACE POWERS MONACO, JD, SAUL GREEN, PhD
- 92 **AIDS fraud, finances, and fringes**
WALLACE I. SAMPSON, MD
- 96 **The physician and cancer quackery—The physician's role in promoting the scientific treatment of cancer and discouraging questionable treatment methods**
IRVING J. LERNER, MD
- 100 **Allergy-related quackery**
WILLIAM T. JARVIS, PhD
- 105 **Fertile field for fads and fraud—Questionable nutritional therapies**
JOHANNA DWYER, DSC, RD
- 109 **Health foods and supplements for the elderly—Who can say no?**
DAPHNE A. ROE, MD
- 112 **Sports nutrition fraud**
SARAH H. SHORT, PhD, EdD, RD, LEONARD F. MARQUART, PhD, RD
- 116 **The role of physicians in dental quackery**
JOHN E. DODES, DDS, MARVIN J. SCHISSEL, DDS

SPECIAL ARTICLE

- 118 **Reflections on the use of unproven arthritis remedies**
JAMES M. STROSBERG, MD

HISTORY

- 120 **Remedies for a society's debilities—Medicines for neurasthenia in Victorian America**
JOHN STEA, MD, WILLIAM FRIED, PhD

(continued on p 64)

(continued from p 3A)

of Medicine, 2701 Stockton Blvd, Sacramento, CA 95817. Tel: (916) 734-5390.

Mar 8-12. Eighth Annual San Diego Postgraduate Magnetic Resonance Imaging Course. 29 Cat I Credits. Hotel Del Coronado, San Diego. Contact: Dawne Ryals, Ryals and Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: (404) 641-9773.

Mar 25-27. Aesthetic Surgery of the Face. San Francisco. Contact: Extended Programs in Medical Education, Registration Office, Room LS-105, University of California, San Francisco, CA 94143-0742. Tel: (415) 476-4251.

COLORADO

Mar 6-13. Update in Clinical Medicine. Vail. Contact: John F. Vargo, George Washington University Medical Center, Office of CME, 2300 K St, NW, Washington, DC 20037. Tel: (202) 994-4285.

DISTRICT OF COLUMBIA

Mar 4-6. Advanced Operative Gynecologic Endoscopy. 21 Cognates. **Mar 15-17. Critical Care in Obstetrics and Gynecology.** 16 Cognates. **Mar 18-20. Management of Breast Disease.** 16 Cognates. **Mar 25-28. Office Gynecology.** 16 Cognates. ACOG Freestanding Postgraduate Courses. Contact: Mary Givens, Registrar, The American College of Obstetricians and Gynecologists, 409 12th St SW, Washington, DC 20024-2188. Tel: (800) 673-8444 ext 2541.

Mar 11-13. Leave No Children Behind: Mobilizing Families and Communities for America's Children. Washington, DC. Contact: Children's Defense Fund, 25 E Street NW, Washington, DC 20001. Tel: (202) 662-3684.

FLORIDA

Mar 8-10. New Frontiers in Medical Care. 11 Cat I Credits. Good Samaritan Medical Center, West Palm Beach. **Mar 22-24. General Surgery 1993.** Contact: Laura J. Keech, CME Coordinator, Good Samaritan Medical Center, PO Box 3166, West Palm Beach, FL 33402-3166. Tel: (407) 650-6236.

NOTICE MSSNY HOD MEETING SCHEDULE CHANGE

Thursday, March 11, 1993: Opening Session has been changed from 1 P.M. to 12 P.M.

YOCON[®]

YOHIMBINE HCl

Description: Yohimbine is a 3a-15a-20B-17a-hydroxy Yohimbine-16a-carboxylic acid methyl ester. The alkaloid is found in Rubaceae and related trees. Also in Rauwolfia Serpentina (L) Benth. Yohimbine is an indolalkylamine alkaloid with chemical similarity to reserpine. It is a crystalline powder, odorless. Each compressed tablet contains (1/12 gr.) 5.4 mg of Yohimbine Hydrochloride.

Action: Yohimbine blocks presynaptic alpha-2 adrenergic receptors. Its action on peripheral blood vessels resembles that of reserpine, though it is weaker and of short duration. Yohimbine's peripheral autonomic nervous system effect is to increase parasympathetic (cholinergic) and decrease sympathetic (adrenergic) activity. It is to be noted that in male sexual performance, erection is linked to cholinergic activity and to alpha-2 adrenergic blockade which may theoretically result in increased penile inflow, decreased penile outflow or both.

Yohimbine exerts a stimulating action on the mood and may increase anxiety. Such actions have not been adequately studied or related to dosage although they appear to require high doses of the drug. Yohimbine has a mild anti-diuretic action, probably via stimulation of hypothalamic centers and release of posterior pituitary hormone.

Reportedly, Yohimbine exerts no significant influence on cardiac stimulation and other effects mediated by B-adrenergic receptors, its effect on blood pressure, if any, would be to lower it; however no adequate studies are at hand to quantitate this effect in terms of Yohimbine dosage.

Indications: Yocon[®] is indicated as a sympatholytic and mydriatic. It may have activity as an aphrodisiac.

Contraindications: Renal diseases, and patient's sensitive to the drug. In view of the limited and inadequate information at hand, no precise tabulation can be offered of additional contraindications.

Warning: Generally, this drug is not proposed for use in females and certainly must not be used during pregnancy. Neither is this drug proposed for use in pediatric, geriatric or cardio-renal patients with gastric or duodenal ulcer history. Nor should it be used in conjunction with mood-modifying drugs such as antidepressants, or in psychiatric patients in general.

Adverse Reactions: Yohimbine readily penetrates the (CNS) and produces a complex pattern of responses in lower doses than required to produce peripheral a-adrenergic blockade. These include, anti-diuresis, a general picture of central excitation including elevation of blood pressure and heart rate, increased motor activity, irritability and tremor. Sweating, nausea and vomiting are common after parenteral administration of the drug.^{1,2} Also dizziness, headache, skin flushing reported when used orally.^{1,3}

Dosage and Administration: Experimental dosage reported in treatment of erectile impotence.^{1,3,4} 1 tablet (5.4 mg) 3 times a day, to adult males taken orally. Occasional side effects reported with this dosage are nausea, dizziness or nervousness. In the event of side effects dosage to be reduced to 1/2 tablet 3 times a day, followed by gradual increases to 1 tablet 3 times a day. Reported therapy not more than 10 weeks.³

How Supplied: Oral tablets of YOCON[®] 1/12 gr. 5.4mg in bottles of 100's NDC 53159-001-01, 1000's NDC 53159-001-10 and Blister-Paks of 30's NDC 53159-001-30

References:

1. A. Morales et al., New England Journal of Medicine: 1221. November 12, 1981.
2. Goodman, Gilman — The Pharmacological basis of Therapeutics 6th ed., p. 176-188. McMillan December Rev. 1/85.
3. Weekly Urological Clinical Letter, 27:2, July 4, 1983.
4. A. Morales et al., The Journal of Urology 128: 45-47, 1982.

Rev. 1/85



Available at pharmacies nationwide

**PALISADES
PHARMACEUTICALS, INC.**
219 County Road
Tenafly, New Jersey 07670
(201) 569-8502
(800) 237-9083



- 127 **The paradise of quacks**
JAMES HARVEY YOUNG, PhD
- 133 **Kindly medicines—A history of the physio-medicals in American medicine**
JOHN HALLER, JR, PhD

CASE REPORTS

- 142 **Diagnosis of occult primary rhabdomyosarcoma by magnetic resonance imaging**
NEIL M. ROFSKY, MD; NANCY B. GENIESER, MD; MICHAEL M. AMBROSINO, MD;
JEFFREY C. WEINREB, MD; KEVIN ROCHE, MD; AARON R. RAUSEN, MD
- 143 **Coronary artery aneurysms—Case report and review of the literature**
TAK KWAN, MD; A. DINO PAIUSCO, MD; C. V. R. REDDY, MD; ALAN FEIT, MD
- 146 **Immunoglobulin-A plasma cell dyscrasia in a young Hispanic man**
HANS W. GRUNWALD, MD; FRED ROSNER, MD; ANDREA C. KALMAN, RPA-C
- 147 ***Salmonella choleraesuis* bacteremia and endocarditis in a patient with acquired immunodeficiency syndrome**
DANIEL D. BUFF, MD; AKSHAY D. PATEL, MD; RICHARD B. NECHES, MD

LETTERS TO THE EDITOR

- 150 **A strong commitment to the *New York State Journal of Medicine***
MARSHALL A. LICHTMAN, MD
- 150 **The fine national reputation of the *New York State Journal of Medicine***
FRED ROSNER, MD
- 150 **The importance of the *New York State Journal of Medicine* to the Medical Society**
LUCRETIA McCLURE
- 150 **A suggestion for the *New York State Journal of Medicine***
ALEXANDER K. C. LEUNG, MBBS; WILLIAM LANE M. ROBSOM, MD; SULAKHAN
CHOPRA, BSC
- 150 **Foamy histiocytes and lepra bacilli in a lymph node aspirate**
MICHAEL KHINE, MD
- 151 **The one white shirt**
RANDALL D. BLOOMFIELD, MD
- 151 **False-positive mammographic imaging of a breast implant**
ROBERT CUCIN, MD, ROBERT BARD, MD
- 152 **Gouty arthritis following gunshot wound**
DAN S. REINER, MD; EDDYS DISLA, MD; ANGELO TARANTA, MD

ESSAY REVIEW

- 154 **Tarnished folk heroes in the battle against AIDS**
WALLACE I. SAMPSON, MD

3A MEDICAL MEETINGS AND LECTURES

We don't
believe
one loss
should
automatically
lead to
another.

Being accused of professional negligence in your treatment of a patient is bad enough. For a medical liability company to compound the charge by automatically cancelling or surcharging your policy is grossly unfair. Unfortunately, some insurers consider even one claim (no matter how unfounded) as reason enough to cancel your coverage.

At MLMIC*, we treat policyholders better than that. We won't cancel or surcharge a policy on the basis of claims history without first submitting it for review to a panel of consulting physicians. Because of the success and strength of our Cooperative Peer Review system, the New York State Insurance Department does not require MLMIC to use an automatic surcharge schedule. *We are the only medical liability carrier in the state with this advantage.*

MLMIC also has the country's largest and most experienced professional liability claims department, as well as New York State's largest risk management department.

Call 1-800-ASK-MLMI (metro) or 1-800-356-4056 (upstate) for more information and an application.

*The only medical liability insurer approved by the Medical Society of the State of New York. Physicians protecting physicians since 1975.



PROFESSIONAL LIABILITY
INSURANCE POLICY
(Claims Made Form)

DPIC
Doctors Protective
Insurance Company

CANCELLED

NOTICE
This is a claims made policy with coverage limited to claims made against you by a third party and have provided, in the course of your practice. You must have provided professional services on or after the retroactive date and before the end of the policy period during the policy period or within 60 days following termination of the policy. Please read your entire policy, as it contains numerous interrelated sections and

MLMISC

Medical Liability
Mutual Insurance Company

Our defense never rests.

250 Harrison St., Syracuse, NY 13202 • 315-428-1188
2 Park Ave., New York, NY 10016 • 212-576-9800
90 Merrick Ave., East Meadow, NY 11554 • 516-794-7200

You'll love working with our
locum tenens physicians and
allied health care professionals.
WE GUARANTEE IT.

CompHealth has thoroughly credentialed physicians and allied health care providers from more than 40 fields of specialization available to provide locum tenens, or temporary, staffing assistance when and where you need it.

Plus, we have the standards and experience to guarantee your satisfaction each time we place a member of our medical staff in your practice or facility. It's the closest thing you'll find to a risk-free way to cover for absent staff members, "try out" a potential new recruit, or take care of your patients while you search for a new full-time associate.

Call us today to arrange for quality locum tenens coverage, or to discuss your permanent recruiting needs.

CompHealth

COMPREHENSIVE HEALTH CARE STAFFING

1-800-453-3030

Salt Lake City ■ Atlanta ■ Grand Rapids, Mich.

**AIM
HIGH**

**BE AN AIR FORCE
PHYSICIAN.**

Become the dedicated physician you want to be while serving your country in today's Air Force. Discover the tremendous benefits of Air Force medicine. Talk to an Air Force medical program manager about the quality lifestyle, quality practice and 30 days of vacation with pay per year that are part of a medical career with the Air Force. Find out what it takes to qualify. Call

USAF HEALTH PROFESSIONS
TOLL FREE
1-800-423-USAF



PRACTICE OPPORTUNITIES

CARDIOLOGY:	Arizona.
EMERGENCY MEDICINE:	Illinois and Wisconsin.
FAMILY PRACTICE:	Upstate New York, Illinois, Wisconsin, Michigan, Iowa and Arizona.
INTERNAL MEDICINE:	Wisconsin, Illinois, Minnesota, Arizona and California.
NEUROLOGY:	Upstate New York.
OG/GYN:	Upstate and Long Island New York, Ohio, Illinois, Wisconsin and Arizona.
ORTHO SURGERY:	Upstate New York, Illinois, Wisconsin and Arizona.
PEDIATRICS:	Ohio, Michigan, Wisconsin and Arizona.
PM & R:	Wisconsin.
PSYCHIATRY:	Ohio, Wisconsin.
UROLOGY:	Wisconsin.

All inquiries are confidential. For additional information call:

GIELOW ASSOCIATES, INC.
1-800-969-7715

WANT DISCOUNTS ON YOUR EXISTING INSURANCE?

We provide complimentary 2nd opinions on your disability and life insurance to provide you with the lowest rates. Servicing physicians exclusively. References provided upon request.

Paul R. Sheinkopf
Sheinkopf & Associates
EAB Plaza West, 5th floor
Uniondale, NY 11556-0137

516-357-8700

FAX 516-357-8891

SELLING YOUR PRACTICE? NEED A BUYER NOW?

Countrywide can provide you with the largest network of qualified buyers and a transaction to secure the best possible price and terms for your practice. Countrywide has helped hundreds of your colleagues buy and sell their practices. To learn how we can do the same for you, call us today at (800) 222-7848.

Countrywide Business Brokerage, Inc.
319 East 24th Street, Suite 23-G
New York, NY 10010

OFFICE SPACE AVAILABLE

Established Medical Arts Building, fully-rented since 1966, in south end of Fort Lee, near Winston Towers. Elevator service. Private parking in rear for doctors. Abundant patient parking in front of building. Centrally located between hospitals.

Large suite—waiting room, two examining rooms; business office; two private offices and/or consultation rooms; rest room. Partitions can be changed easily and modified if necessary. Can be shared by different practitioners or specialists. Had been used as an Ophthalmologists' office with 20 ft. refraction room. Has been shared by Cardiologist, Internists and Urologists. Ideal opportunity for any of these specialties. Currently no Internist in building. Great potential for an Internist. Since services are in great demand, a large practice could be developed as has been done in the past.

For more details call:

Dr. Angelo R. Lombardi
(201) 224-3600

or **Dr. George Azzariti**
(201) 224-3200



COMMENTARIES

Wolves in sheep's clothing

How do you spot a wolf in sheep's clothing? The wolves are always out there, but the information in this issue of the *Journal* will help physicians and other health care providers make consumers more alert to them. In Maslov's hierarchy of needs, basic human survival is our primary motivation.¹ Good health is close to man's most important need. "Wolves," both fraudulent and just plain wishful thinkers, take advantage of people's intense desires, causing them to grasp at straws and listen to empty promises. The public is fleeced \$30 billion annually by the wolves of health fraud.

The New York State Health Fraud Advisory Council was pleased to assist in the preparation of this thematic issue of the *Journal*. The authors are all experts in their fields and provide a wealth of practical information. James Harvey Young in his excellent historical review of quackery shows that, "America may still be a paradise of quacks." The paper by Lerner discusses the physician's role in promoting scientific treatment of cancer. He concludes that "encouraging scientific medicine and discouraging questionable treatments is tantamount to practicing sensitive, caring, quality medicine."

Jarvis's paper, "Allergy-Related Quackery," portrays allergy quacks as both victims and victimizers. He states that "Practitioners who hold misbeliefs about allergies and do not use proper scientific methods can easily be fooled by a combination of their expectations and their patient's responses."

In Strosberg's paper, "Reflections on the Use of Unproved Remedies," physicians are challenged to review any alternative treatment with the patient including possible harmful effects. Concurrently, it is an opportune time to educate the patient as to the unproven claims of the treatment. Strosberg appropriately concludes "although unproven remedies will always be available, there is much we as physicians can do to protect our patients."

Sufferers from diseases such as the acquired immunodeficiency syndrome (AIDS), arthritis, and cancer, for which there may be no known cures, are particularly vulnerable to fraud. In addition, the Food and Drug Administration has also identified the following most

common forms of health fraud: instant weight loss schemes, fraudulent sexual aids, false nutritional schemes, baldness remedies, and other appearance modifiers. Health fraud includes worthless products and services acclaimed by those promising miracle cures they cannot deliver. Myths and magical nostrums are available from adolescence to seniority. Statistics indicate that 50 million Americans will go on a diet this year; however, only five percent will be successful.² In spite of advanced scientific and medical technology, all claims to effortlessly lose weight are false. Yet billions of dollars are spent on diet programs annually. Before the past decade, self-styled "experts" best exemplified by the late Adele Davis were the major source of nutrition advice. Today, scientific and sensible approaches to nutrition are available from licensed or registered dietitians. Physicians should guide their patients to these credentialed professionals rather than to someone claiming to be a "nutritionist." In the Great American Medicine Show, Elizabeth Armstrong concludes "Despite government and professional regulation, you will continue to see Americans seeking out alternative therapies, especially ones that offer hope where traditional medicine has failed."³ Folklore tradition may predispose someone to be anti-scientific. However, physicians should be sensitive to cultural influences, which should not be confused with fraud. For example, in the May 1992 issue of the *Journal*, Rosner describes a *segulah* or nostrum which has a place in traditional Jewish practice alongside scientific medicine.⁴

Today's sensitive and caring physician is supported by the many organizations, both public and voluntary which comprise the New York State Health Fraud Advisory Council. It is the mission of the Council to inform and educate the public about health fraud, to work with appropriate public and volunteer agencies to eliminate the promotion of health fraud and to support and encourage a New York State legislative program to combat health fraud. Established in 1990, the Council's major efforts have been directed towards education. A resource directory is available. A complete listing of council members and other sources of health fraud

activity can be found elsewhere in this issue of the *Journal*. Specific questions of health fraud can be directed to the appropriate organization, one of the consumer groups, or to the New York State Department of Health.

In his proclamation for Health Education Week in 1991, Governor Mario M. Cuomo noted: "The best protection against health fraud is for people to become well informed and skeptical consumers. They must learn to evaluate health claims, to recognize the advertising and labeling ploys that are tip-offs to health fraud, and to report cases of health fraud to the appropriate governmental agencies and business associations." Health care professionals are in a unique position to help in this education process. They need to know nine ways to spot a quack:⁵

- The quack promises quick, dramatic, miraculous cures.
- The quack uses imprecise, non-medical language in his claim.
- The quack uses anecdotes and testimonials to support his claims.
- The quack recommends a wide variety of substances similar to those found in your body.
- The quack recommends that everybody take vitamins or health foods or both.
- The quack's credentials aren't recognized by the scientific community.

- The quack encourages patients to lend political support to his treatment methods.
- The quack tells you not to trust your doctor.
- The quack claims that he's persecuted by the medical community or that his work is suppressed because it's controversial.

To escape from the "wolves" of health fraud, patients should be offered the following advice, "If it sounds too good to be true, it probably is."

RICHARD H. LANGE, MD
Chairman, New York State Health
Fraud Advisory Council
New York State Department of Health
Empire State Plaza
Corning Tower, Room 1455
Albany, NY 12237-0002

1. Maslov AH: *Toward a Psychology of Being*. Princeton, New Jersey, Van Nostrand, 1968.
2. The facts about weight loss: Washington, DC: Federal Trade Commission, Food and Drug Administration, National Association of Attorneys General, 1992.
3. Armstrong D, Armstrong EM: *The Great American Medicine Show*, New York, Prentice Hall, 1991.
4. Rosner F: Pigeons as a remedy (*Segulah*) for jaundice *NY State J Med* 1992; 5:189-192.
5. Herbert V, Barrett S: *Nutrition forum*. 1986; 3:9:65-68.

Combatting medical fraud

As a protector of consumers and promoter of public health, the Food and Drug Administration (FDA) has several levels of concern about medical fraud. They range in urgency from unsafe products that pose a direct threat to health to ineffective medicines that distract patients from medically proven treatment and to ever-present weight reduction nostrums that hurt mostly the consumer's expectations and pocketbook. All unapproved medications, however, violate the law which stipulates that drugs cannot be marketed unless FDA finds them to be safe and effective for their intended use.

The harm caused by products that do not meet these standards is widespread and pervasive. According to an FDA survey conducted a few years ago, an estimated 38-40 million Americans try fraudulent remedies each year, and one of ten users suffers from side effects. The social cost of needless suffering and damage to health is compounded by the high economic toll extracted for unapproved and ineffective remedies. The estimated \$30 billion that Americans expend annually for such medications and devices place an unwarranted burden on top of the more than \$738 billion our nation spends on legitimate health care.

Over the years, FDA—in cooperation with state and local authorities—has fought health fraud by initiating thousands of enforcement actions. The prosecutions of the promoters of Krebiozen and Laetrile are only two landmark examples of FDA's insistence of the highest standards of safety and efficacy for medicines, in spite of occasional, highly emotional protests by believers in unapproved remedies. Last year alone, FDA initiated more than 70 seizures of fraudulent substances ranging

from anabolic steroids and "fountain of youth" palliatives to a "serum" purported to cure both cancer and acquired immunodeficiency syndrome (AIDS). In addition, hundreds of warning letters were sent to promoters of products of dubious therapeutic value.

In recent years, however, while FDA's resources have become increasingly strained by new statutory requirements and escalating workloads, illicit promoters have been expanding their operations across national boundaries. The "fountain of youth" ring broken up last year, for instance, was part of a growing international black market in anti-aging products whose sales in the United States were estimated at two billion dollars a year. It has become clear that the agency's effectiveness against health fraud can only be improved by still closer cooperation with other authorities at all levels of government.

FDA has started this process by establishing a special Health Fraud Unit and entering into partnership with the National Association of Attorneys General (NAAG) and Association of Food and Drug Officials (AFDO).

The thrust of the new policy is two-fold. One major function of the partnership is to coordinate more closely with FDA, state or local regulatory actions against specific health fraud targets. The Health Fraud Unit, which operates a computerized data base on fraudulent health products, helps organize joint or mutually assisted enforcement actions and serves as liaison with interested federal, state and other agencies. This effort is aided by the recently established FDA criminal investigation offices in six major cities, whose specially trained agents will be involved in investigation of health fraud that violates criminal statutes.

The other key goal of the FDA/NAAG/AFDO partnership is to deflate exaggerated claims made for injurious or ineffective remedies and generally increase public awareness of the dangers of quackery. The Health Fraud Unit will support this effort by disseminating health fraud intelligence data and other information for use in press releases and educational activities by cooperating agencies. Acting on the premise that truthful information is the best weapon against illicit operators, FDA plans to hold several Health Fraud conferences, the first one of which, slated for next year, will be designed for the Hispanic community.

As always, FDA remains fully committed to providing the public with the broadest selection of safe and

effective therapies, safe cosmetics and safe and wholesome food. However, our responsibility and the nation's need for combatting health fraud has never been greater. We count on the health care community and the general public to report fraudulent remedies either to the nearest FDA district office, or to the Health Fraud Coordinator, FDA Office of Regional Operations, HFC-151, 5600 Fishers Lane, Rockville, MD 20857.

JANE E. HENNEY, MD
Deputy Commissioner for Operations
Food and Drug Administration
US Department of Health and Human Services
Rockville, MD 20857

FROM THE LIBRARY

THE PROSECUTION OF QUACKS

A warrant was issued for the arrest of one Rafael Cardamone, of East New York. After two adjournments he waived examination for trial at Special Sessions. This case was reported by a citizen of Brooklyn, on his own behalf, and the arrest was made upon his affidavit alone. No detectives were required. The eastern section of Brooklyn is filled with these unlicensed foreigners, and it is rather remarkable we do not receive more complaints from respectable physicians in that vicinity. Henry Surson, of 130 East 123rd Street, who was arrested and accused of practicing medicine without a license, was sentenced yesterday in Special Sessions Court to thirty days' imprisonment and fined \$100.

LEGAL NOTES
(*NY State J Med*) 1903; 3:166-167.

Recognizing deception in the promotion of untested and unproven medical treatments

GRACE POWERS MONACO, JD, SAUL GREEN, PhD

Bravado, self-adulation, ready wit, double tongue, shrewdness, knowledge of the foibles of men, blunted conscience, and ignorance of the subject in which they claim competence are the characteristics of the promoters of "unproven and untested" remedies.¹ Shrewd use of recognized but little understood scientific and medical terms creates an illusion of expertise in the science on which the promoted product is said to be based. This contrived aura of scientific expertise coupled with entrepreneurial shrewdness makes the sales pitch for "cures and eternal good health" very hard to resist.

Over a quarter of the American public has used unproven products^{2,3} ranging in cost from \$300 a month for nutritional supplements to \$30,000 for a course of treatment.⁴ The frightened and vulnerable are the most common targets.^{1,5} Promoters traditionally appeal to the hopelessness of patients faced with what they believe is an incurable disease, play on the fear of the side effects of proven treatments, provide hallelujah testimonials, denigrate the physician as behind the times, and focus on a common belief that natural products have no toxicities or side effects.^{1,5-6}

Those attracted are not only patients who have exhausted proven therapies or clinical trial options, but also nervous individuals who wish to cover all bets in case their therapy does not work. Since ethical physicians cannot say they are cured until they are, fear motivates trying everything that implies it might help. If the condition does not reappear, the patient may become a shill for the unproven "real" cure.^{1,2,5-10}

Physician Trust and Patient Disclosure as Buffers Against Health Fraud. The physician must be the first line of defense against health fraud.^{1,3,5-9} Physicians cannot anticipate health product problems without full patient disclosure of the information they are bombarded with in infomercials, the media and from relatives and friends.^{1,3,5-8}

Patients expect a respectful response^{6-7,9-11} to their inquiries about whether these remedies have been tested, will help them or whether they have been disproved.^{1,3,5-7} Such a collaborative relationship assures patient disclosure of information and facilitates identification of misinformation, inappropriate, and potentially damaging interventions. On occasion, it may lead to the discovery of a valuable complement to care.^{6,10-11} Discovering the misinformation requires constructive listening in an open, communicating doctor/patient relationship.^{1,3,6,11} Inquiries into

patient concerns about diet, nutrition, and media information indicates interest, a willingness to listen and empowers the patient to become an informed medical consumer, alert to the "hype" of promotional health fraud. Physician inquiry encourages patient inquiry.^{1,8,12} It could alert both, for example, to the promotion of questionable use of nutritional supplements to counter the "faulty" American diet⁸ or to affect longevity or the immune system.¹ It alerts both to dangerous "hygienic" measures such as coffee enemas and high colonics.

COME ON'S

Patients, family, friends, neighbors may be seeing adds in the popular media that convey the message: chemotherapy, radiation, and surgery have not touched the cancer epidemic. Promotions for their suggested "alternatives" usually contain some of the following phrases, claims and tactics:^{1,7,8,13}

- Cure, miraculous, nontoxic, conspiracy to suppress; testimonials with no names or objective medical record materials;
- A jump from ambiguous animal studies to use in patients;
- "World authorities," "internationally renowned experts" and "respected scientists;"
- Collaboration with international scientists and extensive foreign studies;
- Ingredients of their product is kept "secret" to prevent theft by the "establishment;"
- "Non-invasive" diagnostic tests can detect cancer, degenerative diseases and subclinical disease otherwise impossible with tests used by establishment doctors.

Promoters' tactics to convince patients not to discuss "their" remedies with their physician may include the following:

- Discrediting proven therapies and those under clinical investigation— "Clearly, the best way to treat (fill in recent fad disease) is first to do nothing orthodox,—that is, nothing harmful."
- Don't cut, burn or mutilate until you have tried our all natural, non-toxic remedy to (fill in disease).
- Don't tell your physician about our treatment—he won't understand it and he will interfere with your trust in our program. Faith is essential to its success.
- Don't use any of the approaches your primary care physician recommends because they all employ unnatural chemicals which will damage your immune system, mask the real cause of your disease and further poison your body.
- Mention a few of these books and articles to your doctor. If he hasn't heard of them, it shows that he is not in the forefront of holistic medicine and wouldn't understand this treatment.

HOW THE PUBLIC IS FOOLED BY THE HYPE FOR THE INTERVENTION

Promotional health fraud hides behind the terms "alternative" or "complementary" medicine.^{7,8,9} Interven-

From the Medical Care Ombudsman Program, Washington, DC (Ms Monaco) and Zol Consultants, New York City (Dr Green).

Address correspondence to Dr Green, Medical Care Ombudsman Program, 123 C St, SE, Washington, DC 20003.

tions properly called "alternative" have been shown to have worth in traditional medicine, in folk lore or in innovative modern medical programs. Complementary suggests that the intervention can augment, assist, or enhance the effect of a treatment already going on. Therapies that have not shown worth by objective standards are not truly "complementary." At best, they are "unproven and untested;" at worst, they are fraudulent and quackery.

A judicial definition of an "unproven and untested" therapy is one that "has not been developed based on a well designed and ongoing program of research, experimentation and study which can be expected to ultimately add to the body of scientific and medical knowledge."¹⁴

Freedom of choice is the promoters ultimate weasel phrase. It means unfettered freedom to take a clients money based only upon the "version" of the facts about their treatment that the promoters choose to disclose. It is the ultimate violation of informed consent^{9,15} since a patient's decision is based upon "managed" information. It means freedom of promoters to be free of responsibility to patients! It does not meet the informed consent standards of the American Medical Association's Patient Bill of Rights. A fully informed medical decision weighs the relative merits of a therapy after full disclosure of risks, benefits and alternatives.

Promoters of "unproven and untested" remedies do not publish negative data. They do not comply with the onerous but ethically essential task of exposing their experimental and clinical results to independent peer criticism. They claim a "conspiracy" prevents them from publishing but rarely can prove that they have submitted their data to peer reviewed journals. They persist in using brochures, throw-aways, popular media articles and TV and radio talk shows as their publications.¹³

A PROCESS FOR THE REVIEW OF "UNPROVEN AND UNTESTED" MEDICAL INTERVENTIONS

Structure of the review process:

Objective. The same considerations apply here as do when you consider referring a patient for a specialized treatment. Your review objectives are to develop materials which will support a dialogue that explains, considers and respects the patients' need to know. The dialogue covers what does the patient expects from this approach; what has the patient been led to believe this approach can deliver; how realistic is the achievement of these objectives?

Data/Sources. Initial data for a review are found in materials provided by the promoter. Supplemental data can be obtained from a Medline search or requested from any of the following: Cancer Information Service (1-800-4-CANCER), American Cancer Society (1-404-320-3333), Candlelighters Childhood Cancer Foundation (pediatric cancers only; [1-800-366-2223], National Council Against Health Fraud Resource Center (1-800-82-6671) and the American Medical Association. An excellent overview of most of these remedies is Congressional Office of Technology Assessment, Report on Unconventional Cancer Treatments: *Unconventional Cancer Treatments*. 1990. Office of Technology Assessment, United States Congress, Washington, DC 20510-8025. Additional information sources are the department of health and the state medical board. Check whether the approach has been reviewed by Consumers Union or the American Council on Science and Health, both in New York City.

The Evaluation Process. The process described here was conceived, developed, and evaluated under a National Cancer Institute grant⁴ to review the most commonly used unconventional biochemical, immunologic, dietary, herbal and botanical approaches to the treatment of cancer. The completed reviews were subjected to outside peer review applying stringent evaluation criteria.

The validity of claims is easily verified. A letter requesting information will usually bring a flood of response mail. The layman is impressed with science so promoters include many references to work published by scientists. When the identity of the scientific basis for the claim is disclosed, a computerized literature search can complete the picture. This process makes the claimant entirely responsible for the conclusions reached by an evaluation. Verification of credentials or data in foreign or out of print journals can be accomplished by a letter to an author of the research cited or the appropriate agency. Promoters rarely expose themselves to the scrutiny of a true peer review process. They "publish" their findings in books for the lay public divorced from the rules of evidence which are obeyed by scientists. The books may contain unverifiable medical records, testimonials from unidentified patients or citations to unsupported statistical evaluations to prove safety and efficacy. Unlike the standard practice of medical scientists who weigh and then report the risks of a treatment as compared to its probable benefit, promoters of quackery never describe untoward effects or fatalities. Their books are thereafter cited as the scientific publications which support their claims that the remedy is safe, effective, inexpensive and a viable alternative to standard medical interventions.

The Process Applied. This process of data collection and evaluation is illustrated below for some aspects of two "untested and unproven" treatments described in promotional books: (1) biologically guided chemotherapy and (2) chelation therapy. Page constraints preclude a complete review.

Biologically Guided Therapy for Cancer—Emanuel Revici.¹⁶ Biologically guided cancer (BGC) therapy is offered to patients in New York City by Emanuel Revici, MD. Among the diseases he claims to treat successfully are cancer, AIDS, heart disease, mental retardation and alzheimers.¹⁶ Revici's claims are summarized in a 1961 book,¹⁶ a transcript of a Congressional public hearing,¹⁷ two papers on the cause and cure of AIDS,¹⁸ a paper on the cause and treatment of radiation injury,¹⁹ and a 1986 US Patent²⁰ describing preparation of the 31 compounds he uses in treatment.¹⁰ Revici's numerous claims include the following:

Twin Formation. Revici said, in 1946, they found a way to determine the electrical charge of atoms in a molecule and determined that two atoms with the same electrical charge could exist bound together. He called this a twin formation.^{16(p242)}

Trienic Forms. Revici states^{17(pp26-37)} that because he could not find a definition for lipids in the scientific literature which satisfied him, he made one up which "is related directly to the forces in the molecules." Using this definition, he "discovered" abnormal lipids in the body which contained fatty acids having three conjugated double bonds and named them trienes.

Abnormal Lipids Induced by Radiation.¹⁹ Revici claims that because radiation produces high levels of "abnormal lipids" in animals or men, they died. Accordingly, he says he developed a method for neutralizing these lipids, and he

sent this information to the Radiological Society in London and the Department of Radiation of the United Nations in Vienna.^{17,19}

Treatment for Cancer. Revici's "medicines" are a series of lipids^{17(pp26-37)} containing different elements.²⁰ Most often used is a lipid-selenium complex, which he says allows him to give patients as much as "1 million micrograms" of selenium, even though he recognizes that the National Academy of Sciences²¹ says more than 150 micrograms is toxic in man. If the content of selenium in these lipid complexes is as high as 1.0/g/dose,¹⁷ the absence of toxicity in his patients may be due to the fact that the selenium in this preparation is totally unavailable for use in the body.²²

The pH, Specific Gravity and Surface Tension of Urine are Determinants of the Metabolic State of the Cancer Patient. Revici^{17,19} says disease is "dualistic" (ie, an imbalance between the constructive states [anabolic] or destructive states [catabolic]). In the anabolic condition, sterols predominate; in the catabolic, fatty acids predominate. Since metabolic waste is excreted in urine, an acid urine is due to anabolic activity and an alkaline urine is due to catabolic activity. His treatment is based on a measurement of the pH, specific gravity and surface tension of a sample of a patient's urine.^{17,19} Urinary pH, specific gravity and surface tension can be dramatically altered by a single meal, a medication, exercise, psychological stress, dehydration, disease or alcohol intake. Only a carefully collected 24-hour urine sample has diagnostic value.²³

Chelation Therapy for Coronary Artery Disease and Atherosclerosis. Practitioners calling themselves "orthomolecular physicians" claim that 400,000 patients have been safely given 6 million chelation treatments with ethylenediamine tetraacetic acid (EDTA) for atherosclerosis and coronary artery disease with marked and lasting benefits in 75% to 95%.²⁴ Among others, chelation therapy is said to²⁴ inhibit the aging process, reverse atherosclerosis and gangrene, decrease angina, heal diabetic ulcers, reduce symptoms of multiple sclerosis, Parkinsons, psoriasis and Alzheimers, improve vision, hearing, smell and muscle coordination, decrease need for insulin and the incidence of thrombophlebitis and increase sexual potency.

EDTA binds di- and trivalent metal ions. The strength with which each metal ion is bound to EDTA varies, iron (Fe+++) being the strongest and calcium (Ca++) one of the weakest.²⁵ EDTA was synthesized in Germany in the 1930s. At that time, because citric acid was used to treat heavy metal poisoning,²⁶ EDTA was tried. It was also tried in patients with mitral valve calcification in 1955.²⁷ The hypothesis that calcified arteries could be softened when calcium was removed was tested in patient's with angina pectoris²⁸ but improvement was short lived.²⁹ In 1985³⁰ and 1992,³¹ placebo-controlled and double-blinded clinical trials were carried out for intermittent claudication; no beneficial effect was observed. Supporters of EDTA-chelation claim that the experimental design and procedure were flawed, the blinding code was prematurely broken and the methods of statistical evaluation were unclear.³² Their "evidence" to support these objections was not disclosed. There is no objective evidence in the numerous clinical cases reported that EDTA chelation had any modifying effect on the course of coronary artery disease.

Chelation therapy is usually delivered by an intravenous infusion of EDTA and is said to promote "unclogging" of the patients plaque-blocked arteries. In the 1960s, the action of EDTA was likened to the removal of the rivets

from a steel structure (ie, without calcium) plaque would come apart. Plaque disintegration would then allow widening of the bore of the arteries. In the 1970s,³³ the mechanism described was the removal of ionic serum calcium. This caused a release of parathormone (PTH) which mobilized calcium from the bones (osteoclastic activity) to replace the calcium lost from the serum. A stimulation of new bone formation created a need for new calcium which was mobilized from the soft tissues and artery walls. This caused arteries to soften and plaque to disintegrate. In the early 1980s,²⁴ the chelation of calcium' hypothesis was rejected by proponents and was replaced with the hypothesis that by chelating and removing metal ions, the production of the tissue-damaging free radicals which cause diseases is inhibited.

Review of Claims. EDTA chelation inhibits formation of disease causing free radicals. A literature review on free radical generation by metal ions yielded the following information:³⁴⁻³⁷

- Chelation with EDTA does not reduce or inhibit the free radical generating capacity of iron in the circulation or tissues;³⁴
- Chelation of iron with EDTA stabilizes and prolongs existence of iron in the tissues and body fluids, allowing it more time to generate free radicals;³⁵⁻³⁶
- Vitamin C, which may be given during EDTA-chelation therapy, plays a direct role in the mobilization of iron from stores in the body, thereby increasing the total amount of ionic iron in the blood during chelation therapy;³⁶
- Oxidation of vitamin C by the iron/EDTA complex can result in additional free radical formation.³⁷

The Infusion of EDTA is Safe. Literature on the biochemistry and physiology of EDTA yields the following information:³⁸⁻⁴⁷

- EDTA is a water soluble compound; it cannot get inside tissue cells to chelate the calcium;^{39,46}
- The binding strength of calcium to EDTA is the weakest of all the metals; all trace metal ions in the blood and on the adjoining blood vessel walls will be chelated and removed from the body via the urine before the calcium is chelated;⁴⁰ Intravenous EDTA causes a massive loss of zinc from the body with toxic consequences for the function of the immune system and with a potential for inducing mutagenic changes in rapidly proliferating tissue cells;^{38,42}
- When exposed to EDTA, the *Escherichia coli* in the bowel release their endotoxins into the gut;⁴³
- EDTA is a powerful inhibitor of blood coagulation, its presence in the circulation during the four hour infusion increases prothrombin time and prevents blood clotting;⁴⁷
- EDTA causes changes in the permeability of the membranes of the islet cells in the pancreas therefore insulin requirements of diabetics can be drastically altered and insulin shock induced;⁴¹
- EDTA causes pseudoleukocytosis and abnormal clumping of platelets in the blood of patients with cancer and other chronic diseases.^{44,45}

CONCLUSIONS AND RECOMMENDATIONS

Medicine is the practice of helping people with injurious conditions. Only cartoon physicians claim infallibility. Physicians who adhere to their Hippocratic oath consider the patients' interest paramount. This means that they welcome, expect and encourage questions about appropriate protocols for treatment. Physicians take the initiative in encouraging or setting up second opinions for patients needing to look further. Physicians, rather than being threatened by other viewpoints, realize that their treatment options are expanded and improved through seeking out the opinions of their peers.

The peer-reviewed medical literature and medical newspapers reinforce the importance of peer comment and

suggestions. These publications are full of exchanges among physicians commenting on treatment protocols and research, challenging assumptions and making suggestions. Sometimes these physician to physician exchanges in print are pointed and spirited criticisms. However, physicians publish articles and provide letters to the editor in the hope that they will be commented on. If there is a better approach or an improvement to be suggested in a protocol, finding this out will benefit patients. Physicians engaging in this cross-commentary do not take each other to court for disparaging their reputations or interfering with their businesses by providing commentary on their journal articles.

In contrast, promoters of "untested and unproven" treatments do not appear to welcome comment or criticism. Promoters use the tactic of character assassination and threats of legal action to deter investigation and reporting of activities detrimental to patients and the public interest. These suits are invariably thrown out by the courts⁴⁸ but this is small comfort to those who have to pay lawyers to defend their right to safeguard patients and the public.

A new system is needed which extends the protection from litigation now accorded to peer reviewers for medical programs to persons engaged in finding and reporting misrepresentations and fraudulent practices in health care. Claims of cures are matters of public interest affecting the public health. Open discussion is essential to facilitate fully informed medical choices.^{49,50} Courts have taken judicial notice that persons practicing highly controversial methods of dealing with disease can expect severe and detailed criticism:

There may be no more serious or critical issue extant today than the health of human beings. Given the frailty of human existence, any controversy on the subject must be afforded wide open discussion and criticism so that individuals may make well educated health care choices. This is especially so in cases where serious disease is involved or death is imminent.^{50 p1206}

Obstacles to promoting the public health through speaking out against promotional misrepresentations misleading patients must be removed.

Acknowledgments. Funding for the development of source materials for this paper was obtained under National Cancer Institute (SBIR) 2 R44 CA41953-02, Evaluative Database on "Unproven and Untested" Cancer Remedies (1988-1991).

REFERENCES

- Monaco GP: The impact of the laetrile phenomenon on the legal profession: Technology by experiment or technology by oath helpers. *Jurimetrics Journal of Law, Science and Technology* 1980;1981; 21(2/3):195-225, 285-328.
- Health, Information and the Use of Questionable Treatments: A Study of the American Public. Louis Harris and Associates for the United States Department of Health and Human Services, September, 1987. Study # 833015
- Edinger RN, Schapira DV: Cancer patient insight into their treatment, prognosis, and unconventional therapies. *Cancer* 1984; 53:2736-40.
- National Cancer Institute (SBIR) 2 R44 CA41953-02, Evaluative Database on Unproven and Untested Cancer Remedies.
- Lerner I: The whys of cancer quackery. *Cancer* 1984; 53:815-819.
- Cassileth BR, Lusk E, Strause TB, et al: Contemporary unorthodox treatments in cancer medicine. *Ann Internal Medicine* 1984; 101:105-112.
- Ellison NM: Unproven methods of cancer therapy. *Drug Ther* 1980; 10, 73-76-78, 81-82.
- Herbert VH, Jarvis WT, Monaco GP: Commentary: obstacles to nutrition education. *Health Values* 1983; 7:38-41.
- Holland JC: Why patients seek unproven cancer remedies: a psychological perspective. *CA* 1982; 32:3-7.
- Newport J: Holistic health center orientations and characteristics. *J Holistic Medicine* 1983; 5(2):178-186.
- Lerner M: A report on complementary cancer therapies. *Advances* 1985; 21:31-45.
- Fitzgerald FT: Science and scam: alternative thought patterns in alternative health care. *NEJM* 1983; 309(17): 1066-1067.
- Ellison NM: Cancer quackery: what to watch out for. *Drug Ther* 1980; 10:87-89.
- Odenwall v *Aetna*, Docket K-86-283-CA4 (WD Mich).
- Peters v Dr Harold Manner et al*, Docket 83L 22441 (Ill Cir) (vitamin A toxicity, metabolic therapy, consumer fraud).
- Reveci E: *Research in Physiopathology as the Basis of Guided Chemotherapy with Special Application to Cancer*. Princeton, Van Nostrand Co, Inc, 1961.
- Reveci E: Testimony at a Congressional Public Hearing before Congressman Guy Molinari, March 18, 1988, 26-37, New York, New York.
- Reveci E: Theoretical background and research for treatment of AIDS. *Townsend Letter for Doctors* 1987, Port Townsend, WA, February/March, 8-13.
- Reveci E: Deleterious effects of radiation due to the production of trionic conjugated fatty acids. *Townsend Letter for Doctors* 1989, Port Townsend, WA, January/ February, 12-17.
- Reveci E: A treatment for symptoms of neoplastic disease. United States Patent, 1986, #462485.
- National Academy of Sciences. Recommended dietary allowances. 9th ed. Washington, DC: National Research Council, National Academy of Sciences, 1980.
- Ip C: Interaction of vitamin C and selenium supplementation in the modifications of mammary carcinogenesis in rats. *JNCI* 1986; 77:299-303.
- O'Connor G, Kunau RT: Renal transport of hydrogen and potassium. In Brenner I B, Stein J H (eds): *Acid-Base and Potassium Homeostasis*. New York and London, Churchill Livingstone, Inc, 1978, pp1-30.
- Cranton E, Brecher A: *Bypassing the Bypass*, ed 2. Trout Dale, Virginia. Medex Publishers, 1990.
- Dwyer FP, Mellor DP (editors): *Chelating agents and metal chelates*. New York, Academic Press, Inc, 1964.
- Kety SS, Letonoff TV: Treatment of lead poisoning with sodium citrate. *Proc Soc Exptl Bio Med* 1941; 46:476-477.
- Clark NE, Clark CN, Mosher RE: The in vivo dissolution of metastatic calcium. *American J Med Sci* 1955; 229:142-149.
- Clark NE, Clark CN, Mosher RE: The treatment of angina pectoris with disodium EDTA. *Amer J Med Sci* 1956; 232: 654-666.
- Kitchell JR, Palmon F Jr, Aytan N, et al: The treatment of coronary artery disease with disodium EDTA: a reappraisal. *Amer J Cardiology* 1962; 11: 501-506.
- Diehm C: The wonder remedy-chelation: a clinical trial. *Zeitschrift d Deutschen Herzstiftung Heft* 1986; 10: 11-15.
- Culdager B, Jelles R, Jorgensen SJ, et al: EDTA treatment of intermittent claudication—a double blind, placebo controlled study. *J Int Med* 1992; 231: 261-267.
- Letter to the Editor from J. P. Frackelton, President, American Institute of Medical Preventives, *Townsend Letter for Doctors*, Port Townsend, WA, July 1992; 604-605.
- Walker M, Gordon G: *The Chelation Answer*. New York. M Evans and Co, 1982.
- Green S, Mazur A, Shorr E: Mechanism of the catalytic oxidation of adrenalin by Ferritin. *JBC* 1956; 220:237-255.
- Prigodich RV, Martin CT: Reaction of single stranded DNA with hydroxyl radical generated by iron (++)MEDTA. *Biochemistry* 1990; 29:8017-8019.
- Gutteridge JMC, Halliwell B: Iron toxicity and oxygen radicals in Bailliere's. *Clin Hematol* 1989; 2:195-256.
- Alcain FJ, Buron MI, Rodriques-Aquilar JC, et al: Ascorbate free radical stimulates growth of human promyelocyte leukemia cell line. *Cancer Research* 1990; 50:5887-5891.
- Brownie CF: Teratogenic effects of CA-EDTA in rats and the protective effect of zinc. *Toxicol Appl Pharm* 1986; 82: 426-443.
- Castellino N, Aloj S: Effect of Ca-Na EDTA on the kinetics of distribution and excretion of lead in the rat. *Brit J Indust Med* 1965; 22:172-180.
- Allain P, Mauras P, Premel-Cabic A, et al: Effects of an EDTA infusion on the urinary elimination of several elements in healthy subjects. *Brit J Clin Pharmacol* 1990; 29:347-349.
- Meltzer LE, Palmon FP, Kitchell JR: Hypoglycemia induced with disodium EDTA. *Lancet* 1961; (September) 16:637-638.
- Stich HF, Karim J, Korpatnick J, et al: Mutagenic action of ascorbic acid. *Nature* 1976; 260:722-723.
- Cassidy MM, Tidball CS: Cellular mechanism of intestinal permeability alterations produced by chelation. *J Cell Biol* 1967; 32:685-698.
- Berkman N, Michaeli Y, Reuven O, et al: EDTA dependent pseudo-thrombocytopenia—a clinical study of 18 patients and a review of the literature. *Amer J Hematology* 1991; 36:195-201.
- Savage RA: Pseudothrombocytopenia due to EDTA-induced platelet clumping. *Amer J Clin Path* 1983; 81:317-322.
- AMA Drug Evaluations*. New York, John Wiley and Sons, 1980, pp902-903.
- Klaassen CD: Heavy metals and heavy metal antagonists. In Gilman AG, Goodman AG, Gilman LS (eds): *Pharmacological Basis of Therapeutics*, Macmillan Publishing Co, Inc 1980, pp1620-1621.
- Margaret C. Jacob. *Personal Representative of the Estate of San D. Jacob, deceased v Gregory C. Curt, J.G. Katterhagen, Francis Mahaney, Walter Bond, Ronald St. John, Virginia Knauer, et al*. Docket 88-951 PA (DC Or).
- Farnsworth v Tribune Company*, 253 NE 2d 408, 411 (ND Ill 1969) (medical quackery).
- Spelson v CBS, Inc*, 581 F Supp 1195, 1206 (ND Ill 1984) (defamation and damage to business relating to controversial "metabolic" therapy for cancer).

AIDS fraud, finances, and fringes

WALLACE I. SAMPSON, MD

Human immunodeficiency virus 1 (HIV 1) disease, a social and medical disaster, has produced opportunities for fraud and fraud watchers. As opportunists make small fortunes, we have the opportunity to observe the natural history of pseudoscience and society's responses.

The cast of players is familiar—well meaning self-help organizations, self-deluded and self-important dreamers with gossamer philosophies, and outright charlatans. However, as is usual with medical fraud and pseudoscience, the distinctions are blurred, and many groups feature all three.

BACKGROUND

The major features of the HIV-affected population's response to dubious methods is the high percentage of people who embrace them. Non-standard and ineffective therapies become most popular in the male homosexual community, starting in San Francisco. The initial meager government response to the epidemic boosted many into worthless methods as a reaction against governmental inertia. *The Plague* by Albert Camus¹ is a dramatic teacher. Written as an allegory for the world's inaction to Hitler's rise to power, it traced leaders' foot-dragging when faced with a public health threat few felt would materialize or affect them personally. The book is prophetic of the US government's slow response to the acquired immunodeficiency syndrome (AIDS) despite the warnings of the scientific, public health, and patient activist communities. According to Donald Francis, MD,² and author Randy Shilts³ inertia seems to have been official policy. There is a common perception that many homosexuals and their sexual practices are aberrant, repulsive, or immoral. Gays as well as others with HIV infection, including intravenous drug users and transfusion recipients, became special social outcasts along with their families. Many in the HIV-infected gay communities perceived the medical profession as being grouped with the "Establishment," as objects of mistrust. A minority of physicians who refused to care for HIV-infected people compounded the problem.

In addition, there is the long Food and Drug Administration (FDA) drug approval process that takes years and millions of dollars for a new drug to be approved. During the investigational phase, access is limited to certain subgroups who qualify, and to the limited number selected for each trial. Geographic location also limits access to research drugs.

These factors compounded the frustration of HIV-infected people as well as of physicians witnessing HIV's

devastations. Mistrust resulted in a mass movement out of mainstream medicine. R. Wachter, MD, has outlined much of this history over the last ten years.⁴

Many gays looked to gay physicians to care for them. To their credit, gay physicians stepped in to do so. They often came from unrelated specialties—oncology, dermatology, general medicine, rheumatology—and molded their practices to the epidemic, becoming AIDS specialists.

From early in the epidemic, many infected gay men used other systems such as physical exercises, homeopathy, meditation, and naturopathy. They also looked to nutritional supplements and investigational drugs obtained through black and gray markets, hoping to strengthen their immunity. Buyers' clubs sprang up nationwide to sell chemicals and drugs obtained from manufacturers and renegade secret laboratories. Some "ethical" pharmaceutical manufacturers sold directly to buyers' clubs and guerrilla clinics, violating their standards of commercial behavior, as well as FDA and state regulations.

The situation became so uncontrolled that the FDA and state agencies were unable to deal with it through standard policies. The FDA approved a number of dubious materials and devices for Investigational New Drug (IND) and Investigational Device Exemptions (IDE). This was done to mollify mounting political pressures for access to "alternative" as well as to legitimate investigational methods, and to reduce the work load on the FDA's limited and harried enforcement staff.

The percentages of people who now opt for unproven or worthless methods is not known, and probably varies with affected groups. The most active has been the gay community.

According to Molly Cooke, MD, of the University of California San Francisco, (personal communication, October, 1991) 30%–60% of people enrolled in clinical trials altered their placebo or experimental status by taking unauthorized drugs or changing the doses of what they were given.

There is no effective IV drug users' group, and users have not joined forces with gays. People with transfusion associated HIV tend to act individually or in concert with established medical organizations. The important observation is the gays' extraordinary movement to many unproven and fraudulent methods.

COMMON UNPROVEN AND FRAUDULENT REMEDIES

In 1985, *American Medical News* described the growing market in phony AIDS remedies.⁵ By 1986, the Laetrile/cancer quackery promoters had placed themselves in the AIDS world.⁶ By 1988 John Renner, MD, and this author collected a list of over 200 different remedies and methods offered and sold by stores and various individuals. The Healing Alternatives Foundation of San Francisco now

From the Oncology Division, Santa Clara Valley Medical Center, San Jose, California 95128.

Address correspondence to Dr Sampson, Acting Chief, Oncology Division, Santa Clara Valley Medical Center, San Jose, California 95128.

offers a list of 121 products it supplies by mail. These include vitamin and mineral supplements (seven different forms of vitamin C), amino acids, other food supplements (biotin, Spirulina [three forms] chlorella, germanium), anti-oxidants ("AOX/PLX," "BHI"), "immune stimulants" ("DNCB," levamisole), proposed antivirals (isoprinosine, compound Q-trichosanthin, AL-721), and herbs (Pau D'Arco, astragalus, Valerian root, garlic, ginseng, comfrey, etc).⁷ None of the 121 products has known clinical value against HIV infection or its complicating infections, although some unapproved anti-viral agents are active against HIV or HIV infected CD⁴⁺ T cells in vitro.

In the mid-1980s, the list contained a number of ineffective cancer remedies including vitamin C. The most prominent Laetrile organizations, the Robert Bradford Foundation and the Committee for Freedom of Choice in Medicine (formerly the Committee for Freedom of Choice in Cancer Therapy) have outpatient and inpatient programs for AIDS at their Tijuana hospital.⁸ In spite of these proponents' accusations of the high cost of ethical medical care, their own costs are not low. A week at the Bradford Research Institute Hospital in Tijuana costs \$4,300 with \$300 per month after that. A two-week stay costs \$6,600 with \$400 per month for home medication. Three weeks cost \$9,900 followed by \$450 per month.⁹ This is not inexpensive considering that the treatments are scientifically unproven, highly unlikely to work, or fraudulent.

Bradford spokesman Michael Culbert, a former editor of the *Berkeley California Gazette*, and the author of two books on Laetrile for cancer, has also written books on AIDS¹⁰ in which he develops theories about AIDS and HIV infection also supported by political extremists. They include claims that HIV is not the sole cause of AIDS, that other factors are syphilis, herpes viruses, Epstein-Barr virus, hepatitis, cortisol excess, and cytomegalovirus, and that predisposing factors include venereal infections, substance abuse, syphilis, antibiotic abuse, refined carbohydrates, fluoridated water, vaccinations, "environmental poisonings," and blood transfusions.

Some claim that immune systems may be partially rebuilt by "intervening therapies," and that a positive blood test corresponding to "100% mortality is a thought, not a fact." (Although some HIV positive people may live five to ten years without developing AIDS, most experts agree that HIV infection is ultimately fatal.) These claims are a standard technique of pseudoscience proponents. Because the proponents' explanations and treatments are inconsistent with scientific knowledge, they create mistrust of valid information and encourage belief in their fraudulent substitute system. Bradford and Culbert's statements cast scientific explanations of AIDS into doubt, and prepare the patient for their own extraordinary claims.

Bradford treatments are a mixture of "old metabolic therapy" for cancer and newer methods directed to "boost" the immune system and neutralize the virus. Old treatments include staphage lysate, amygdalin (one form of Laetrile), live cell therapy, herbal teas and enemas, coffee enemas, acidophilus, and chelation therapy with edetic acid. Dietary changes include vegetarian diet, no refined carbohydrates or animal fats or protein, and "detoxifying" with fruits and vegetables. They administer broad spectrum antibiotics and penicillin because signs of advanced HIV were found in neurosyphilis, and "a number of researchers treat AIDS as if it were syphilis."

They also give "immune enhancers:" vitamins A, C, E, B₁, B₃, fatty acids, AL-721, iron, zinc, amino acids, "anti-oxidants" such as catalase, dimethyl sulfoxide, and glutathione, and anti-inflammatory and proteolytic enzymes. Another group includes "oxytherapies:" Hydrogen peroxide, ozone, and organic germanium. None of these methods has been scientifically shown to perform functions or to provide benefits to AIDS patients in the ways claimed.

An administrative and product supply arm of the Bradford Institute, American Biologics of Chula Vista, California has billing and collecting methods for what medical science considers unnecessary and ineffective services. A number of insurance companies have refused to pay, and some patients have brought suit against the companies.¹⁰ A case against American Biologics for falsely claiming to cure cancer and AIDS is now pending with the District Attorney of San Diego County, California.¹¹

State and Federal agencies usually handle violations with letters requesting cessation of the activity—known as compliance letters. Compliance letters are not made public, so that most actions against companies and individuals cannot be reviewed here. However, some other court actions have been taken. One notable case was against an Orange County, California, radiologist who produced a substance he called Viroxan in his kitchen sink and injected it into AIDS patients. He surrendered his medical license voluntarily in 1991. An associate had his medical license revoked, whereupon he sued the Medical Board of California.¹¹ In 1990, the owners of Oasis Purewater, Inc., of San Diego were fined \$500 each and received suspended one-year prison sentences for selling industrial strength hydrogen peroxide for AIDS.¹¹

One former orthopedic surgeon in Los Altos, California, gives massive doses of intravenous vitamin C to AIDS patients, claiming to raise their CD⁴⁺ cell counts and to prolong their lives. He administers doses exceeding 100 mg daily, even though they can cause kidney failure, red cell hemolysis, and death. No one has demonstrated beneficial effects of ascorbate in AIDS patients.

Ozone therapy was given to AIDS patients by flowing blood through an ozone generator and returning the treated blood to the patient. Ozone generators along with some other dubious methods were given IDE status by the FDA. There is no proof of effectiveness for ozone use against HIV in people.

Many "health food" stores misrepresent products. In Houston, Texas, Martin surveyed 41 health food stores by requesting materials to protect the wife of a (fictional) infected husband. All stores claimed to have had HIV preventative products including multiple vitamins, vitamin C, coenzyme Q10, germanium, lecithin, raw glandular extracts, homeopathic remedies algae, hydrogen peroxide, and herbs. None of these is active against AIDS. No store clerk recommended use of a condom.¹²

FINANCIAL MANEUVERS

There are ways to make money without selling a product. One way is to sell stock in a company claiming to have a promising AIDS treatment. This scheme is modeled after stock swindles by Laetrile promoters in the 1970s and 1980s.¹³

In 1987, two physicians and a businessman formed a company with claims of having an apparatus to treat HIV disease. It was a cot with a wiring system that carried a low amperage electric current. The electromagnetic field gener-

ated, along with two wavelengths of blue light that played on the patient from above, were claimed to stimulate CD⁴⁺ cells and improve clinical status. Eight patients were treated without Federal or state approval or permission from an institutional review board (IRB). This activity violated state and federal regulations. They then applied to the FDA for an IDE, using selected data. They claimed most patients improved. At least two consultants to the California Board of Medical Quality Assurance reviewed the raw data and found that the proponents had not reported anemia, weight loss, and other detrimental changes. Often the treatment was stopped when the CD⁴⁺ count happened to be higher during a normal swing, thus seeming to show improvement.

FDA policy at the time was to grant IDEs and INDs for any HIV treatment not likely to be harmful. While local authorities prepared charges against the company for the Attorney General an IDE was granted. The device was then listed in two issues of the American Foundation for AIDS Research directory, numerous publications such as *Insight* and *Pennystock News* carried stories on the device,^{14,15} and the company was featured on local TV news broadcasts.

The stock (several million shares) was owned by the promoters, and sold on penny stock exchanges through brokers in New Jersey and Utah. It rose from \$0.06 to \$0.10 per share in January 1987 to at least \$0.74 per share in March/April 1987, an increase of almost 1,000%. There is no official record of how many shares changed hands. The company obtained a belated IRB approval from Mt Zion Hospital, San Francisco, and arranged for experiments on cats at the University of California, Davis, all after treatments were given to human volunteers. The company moved from an old rented house in Mountain View, California, to an upscale Silicon Valley building in Cupertino.

It subsequently did no more experiments, never marketed the device, considered marketing substances for arthritis, premenstrual syndrome, and other troublesome conditions, and disappeared one to two years later. The IDE expired when the company failed to renew. The HIV patients were not charged, but false hopes were raised and the money was made from stock sales.

GRAY MARKETS AND BUYERS' CLUBS

Perhaps the most difficult area of borderline illegal activities to define and deal with. Because of the social conditions described above, HIV patients have little patience for the FDA and medial system to catch up with their desires for access to potentially beneficial medication. Starting just one year after the identification of HIV, groups of infected individuals and their associates began looking for independent access to unapproved drugs. Project Inform (PI) of San Francisco was among the first. Its activities have been covered in the *New York Times* and the *San Francisco Examiner*.¹⁶⁻¹⁸

Its controversial role derives from its strong influence in the HIV community, the Department of Health and Human Services, FDA, National Institutes of Health (NIH), and with state and local authorities. Yet, its directors are self-appointed and not subject to election by members or by the large gay community they speak for, nor has it any competing organization. Not only does PI negotiate directly with and influence FDA and NIH policy, it co-sponsored and ran the first "community" compound Q trial (GLQ 223, trichosanthin),¹⁹ without the permission of regulatory

agencies. The project was approved by an IRB of its own construction, unassociated with a hospital, university, or other independent organization. One physician who headed the trial is noted for his espousal of "clinical ecology."²⁰

The "Q" clinical trial proceeded while PI was the seller of Compound Q. The trial ended with mixed results, no proven efficacy, two admitted deaths and a number of other toxic reactions. Another controlled trial was apparently devised, and a preliminary Phase I/II trial presented at the VIIIth International AIDS Conference (no conclusion of efficacy). PI continues to supply compound Q commercially and hypes it with its newsletter.²¹

Just as intriguing was PI's role in popularizing dideoxycytidine (ddC), another antiviral drug. ddC is too neurotoxic to take alone in effective doses, but seems to be tolerable at a lower dose in combination with zidovudine. In spite of this, PI was and is a distributor of ddC. It marketed, from renegade chemical laboratories, ddC that was not standardized for content or purity. Lots were found to have next to no ddC activity to two times the amount claimed when analyzed by Hoffman-LaRoche, the manufacturer of ddC.²² PI did nothing to assure potency or purity. Neither Hoffman-LaRoche nor FDA took action. Ordinarily the FDA or state agency would order immediate seizure of the products, or more, and the patent holder, ie, LaRoche, would sue for patent infringement. However, no action was taken until the FDA stopped the trial after three deaths.¹⁶

This situation illustrates the power that PI wields with government agencies and its following. In late 1991, regulatory representatives met with PI and other groups to discuss the situation. They apparently forged a compromise solution. FDA and state agencies would keep a hands off policy for buyers' clubs distributing investigational drugs likely to have some role or anti-HIV effect as long as no dangerous reactions occur.²² In return, PI and others would join in anti-AIDS fraud activities and inform their constituencies about the dangers of quack remedies.

PI has since published a "hot list" of methods to avoid. These include "Auto-immune Viracide" (M. Bilbrey, Phoenix, AZ), Roka's Plant Treatment and Clinic (Switzerland), and the long-time cancer pseudotreatment "antineoplastons" of S. Burzynski of Houston, Texas.²³ A PI member is also a member of the California AIDS Fraud Task Force.

The decision to allow buyers' clubs to operate under FDA's half closed eyes not only allows the clubs to continue and to profit, but helps PI and others to eliminate competition. In addition, the line between fraudulent products and those marketed by the clubs has not been drawn, as is seen by the long list of ineffective products available from the Healing Alternatives Foundation, that works closely with PI. In addition, PI has criticized dissenting individuals and organizations in the press.²⁴ FDA officials are mum on the subject, but the policy has the support of the community at risk. The compromise is felt to be the best FDA can extract.

SELF CARE

A number of self-care methods have been popular from the beginning of the epidemic. These include taking nutritional supplements already mentioned, and various exercises. Many lift weights and use aerobic conditioning. Some delve into parapsychological escapism and "New Age" beliefs. One woman who contacted AIDS from her mate claims to have reverted to sero-negative status through transcendent experience.²⁵

Popular in the mid- and late-1980s was a Los Angeles New Age therapist-philosopher, Louise Hay. She wrote articles and books, and gave seminars (one costing \$7.50 per person) claiming that AIDS is not a fatal disease, and that faith and attitude help to overcome the disease.²⁶ One faith strengthening exercise was to gaze at oneself in the mirror and repeatedly utter complementary phrases and "I am well." She has not been popular recently—perhaps because common sense sometimes prevails.

Another method was organized by a woman who falsely claimed to have a PhD in biology from the University of California at Berkeley. She conducted groups at which HIV affected people sat holding hands, but were instructed not to wear underwear because warm genitals encouraged HIV growth. They also were told to drink only distilled water.

At the VIth International AIDS Conference in San Francisco in 1990, a parallel conference at a nearby hotel was held and organized by Lawrence Badgley, MD, an advocate of alternative therapies. His book, *Healing AIDS Naturally*, promotes homeopathic remedies, meditation, imagery, and a multiplicity of other maneuvers.²⁷

Conquering AIDS Now by S. Gregory and B. Leonardo²⁷ describes other self-care methods from mildly humorous to ridiculous, such as improving immunity by "thumping" on the thymus, and sitting in sunlight with the genitals and anus exposed to sunlight at the recommended angle of 40°. It also recommends "dry brush massage" and "adrenal massage." Although many AIDS patients scoff at such suggestions, some are worried, frightened, and gullible enough to accept them.*

CONSPIRACY THEORIES

An interesting offshoot of the AIDS epidemic is the rise of opposing theories on the origin of the HIV itself, and how it became a human pathogen. At the Whole Life Expo in 1989 in San Francisco, proponents of Laetrile and "live cell analysis" (diagnosing nutritional deficiencies by examining clumping of blood cells in a suspension) told attendees that HIV was introduced into hepatitis B vaccine and smallpox vaccine by the biological warfare unit of the US Army at Fort Detrick, Maryland.

The book, *AIDS: Hope, Hoax, and Hoopla*,⁸ by Laetrile proponent Michael Culbert states that HIV may have been introduced into Africa by World Health Organization smallpox vaccine, or into the United States through hepatitis B and polio vaccine. A recent article in *Rolling Stone*²⁹ claiming that HIV was introduced into Africa by polio immunization was reviewed in *Science*.³⁰ A rebuttal by Hilary Koprowski, a co-developer of polio vaccine, was printed in *Science*.³¹

A Los Angeles gastroenterologist, Robert Strecker, also developed a theory that man-made HIV was intentionally introduced into the gay community via hepatitis vaccine, by agents of the then USSR, with the connivance of the NIH, and into Africa via smallpox and polio vaccines. Strecker and his supporters appeared on a nationally televised program, *Tony Brown's Journal*, during which panelists supported right-wing conspiracy theories. Strecker produced an hour-long video on the subject that he sells nationwide.

Even the Rev Louis Farrakhan and the Nation of Islam have been involved in a crank AIDS remedy. An oral form

of interferon was promoted by Kenyan physicians and hyped by Rev Farrakhan. It was produced separately by two different laboratories and named Kemron and Immunex. A protein, interferon is probably destroyed by intestinal enzymes and not absorbed intact. It has no demonstrable effectiveness against HIV or AIDS outside of the anecdotal claims of its promoters. The claims were accompanied by statements that AIDS is a disease concocted to destroy blacks.³² The interesting aspect to these conspiracy theories is that they all accuse Federal agencies, even the US Army and the Central Intelligence Agency, of conspiring to eliminate segments of the population by stealth or extraordinary incompetence. The effect is consistent with a right wing political agenda to engender mistrust of regulatory agencies. Proponents have not yet won many converts to their causes, but they amplify suspicion and resentment of agencies regulating health fraud. Suspicion of authority is a national characteristic of Americans, and is easily aroused.

CONCLUSIONS

The spread of fraudulent and pseudoscientific methods in the HIV-infected population is a result of resentment of authority, the lack of effective remedies for a fatal disease of young people, and the ready imagination and opportunism of cranks and charlatans, as well as well-meaning yet ambitious individuals. The heady feeling of power may be a strong motivation of people who begin by merely wanting to help or to correct a perceived injustice. In the AIDS scene, the population seems not to want to control the people who may take advantage of them. AIDS has been a wellspring of opportunity for profiteering and for the propagation of pseudoscience.

REFERENCES

1. Camus A: *The Plague* NY, Alfred Knopf, 1948.
2. Heilig S, Donald L, Francis MD: How CDC politics has botched the fight against AIDS. *Calif Phys* 1992; 9:38-41.
3. Shilts R: *And the Band Played On*. New York, St Martins Press, 1988.
4. Wachter RM: Aids, activism and the politics of health. *N Eng J Med* 1992; 326:128-133.
5. Anon: AIDS, patients go to unproved remedies. *Medical World News*; August 22, 1983; p2.
6. Bradford Research Institute information packet, 1991.
7. Healing alternatives foundation product price list. 1992.
8. Culbert M: *AIDS: Hope, Hoax, and Hoopla*. Chula Vista, CA, The Bradford Foundation, 1989.
9. Culbert M: *AIDS. Terror, Truth, Triumph*. Chula Vista, CA, The Bradford Foundation.
10. Anon: *The Choice* 1992; 17:27-28.
11. Department of Health Services, State of California: Report to the 1991 legislature on regulation and control of the diagnosis and treatment of cancer. 1991, p4.
12. Martin N: AIDS fraud rampant in Houston. *Nutrition Forum* 7:16, March/April, 1990.
13. US District Court, Northern District of California. *US v E. Krebs et al*. 1973.
14. Biosystems Research, Inc. Prospectus. May 9, 1987.
15. Non Drug AIDS aid. *Insight*. May 11, 1987:55.
16. Kolata G: Trial of experimental AIDS drug to be continued with revisions. *NY Times* Mar 9, 1991; pA1.
17. Krieger L: Top AIDS activist: leader or tyrant? *San Francisco Examiner* Sept 8, 1991; pA1.
18. Garrison J: Q still unproved in AIDS drug tests. *San Francisco Examiner* March 7, 1990; pA1.
19. Byers V, et al: A phase 1/II study of trichosanthin treatment of HIV disease. *AIDS* 1990; 4:1189-96.
20. Huber P: *Galileo's Revenge, Junk Science in the Courtroom*, Basic Books pp164, 179, 194.
21. Project Inform Fact Sheet. May 15, 1991.
22. Krieger L: Underground AIDS drug under probe. *San Francisco Examiner* Jan 29, 1992; pA1.
23. Project Inform hot list. Jan 13, 1992.
24. Dobson J: Bad activists and yellow journalists. *San Francisco Sentinel* Sept 12, 1991; p11-12.
25. Asistent N: Why I survive AIDS. *New Age Journal* Sept/Oct, 1991; pp38-41, 109-120.

*For an excellent and thorough review of the major alternative treatments most popular with AIDS patients until 1990, see Abrams DI: Alternative therapies in HIV infection. *AIDS* 1990; 4:1179-1187.

26. Hay L: *You Can Heal Yourself*. Self published, Los Angeles, 1987.
27. Badgley L: *Healing AIDS Naturally*. Humana Energy Press, 1987.
28. Gregory S, Leonardo B: *Conquering AIDS Now*. Santa Monica, Tree of Life Publications, 1986.
29. Curtis T: The origin of AIDS. *Rolling Stone*, March 1992.

30. Cohen J: Debate on AIDS origin. *Science* 1992; 257: pp1024, 1026.
31. Coats C: The Nation of Islam announces AIDS cure. *Voice and Viewpoint*, June 4, 1992, p1.
32. Clark C: Muslim tells of powerful AIDS fighter. *San Diego Union-Tribune* May 19, 1992, ppB1, 4.

The physician and cancer quackery

The physician's role in promoting the scientific treatment of cancer and discouraging questionable treatment methods

IRVING J. LERNER, MD

The promotion of questionable methods of treatment for cancer and other serious illnesses clearly is a very longstanding phenomenon. Only relatively recently have investigators begun to analyze the dynamics of the phenomenon (eg, what are its characteristics?, who promotes it?, who uses it?, how prevalent is it?, how harmful is it?, and is there any value to it?). Studies about questionable treatments have consistently demonstrated a distressingly large number of medical physicians among the purveyors.¹ In contrast, relatively little attention has been directed to the role of the scientific physician in dissuading patients from questionable treatments in favor of proven treatments. There is at least the implication that the treating physician may be pivotal in influencing patient decision-making in this fundamental area.²

Questionable treatments of cancer can be defined as treatment methods which are promoted for use, but which have not met the safety and efficacy requirements of the United States Food, Drug and Cosmetic Act. Safety and efficacy are established by providing reproducible scientific data according to well-recognized methodologies. In contrast to questionable treatments, legitimate investigational treatments are those which are currently under study for safety and efficacy and consequently are not promoted for general use.

The American Cancer Society has long been the repository of information regarding questionable cancer treatments. In addition to cataloging these, in recent years the Society has made the additional effort to try to grade them according to their prevalence and their perceived risk to the user (Tables I and II). Cassileth and Brown observed that contemporary questionable treatment methods tend to differ from earlier specific "pills or potions, in that they are life style oriented remedies."³ One notes a marked increase in dietary promotions, alleged alterations of the immune system, and mind therapies.

PREVALENCE

In an effort to determine the prevalence of questionable cancer treatments in the United States, the American Cancer Society commissioned a random digit dialing telephone survey of 36,000 American households, ultimately querying more than 5,000 individuals.⁴ It was the conclusion of this survey that questionable cancer methods were utilized nine percent of the time nationwide. Similar data

from smaller or more regional surveys of the population have yielded prevalence figures ranging from 6% to 23%.⁵⁻¹⁰ It should be noted there were marked regional differences in the use of questionable treatment methods, with the rate exceeding 15% of cancer patients in Minnesota, Massachusetts, Connecticut, Oregon, Idaho, New Mexico, and Delaware, and involving less than five percent of cancer patients in Illinois, Virginia, Louisiana, Oklahoma, Missouri, West Virginia, South Carolina, New Hampshire, Iowa, and Rhode Island.⁴

CHARACTERISTICS OF USERS

Although one might have anticipated that less affluent and less educated individuals might be more vulnerable to the seduction of questionable cancer treatments, in fact the opposite is the case. The American Cancer Society's survey⁴ demonstrated a nearly linear correlation between higher income or higher education and questionable cancer treatment use. Among cancer patients residing in households with an income of more than \$50,000, 13.2% used a questionable treatment method in contrast to 6.6% in households whose incomes were less than \$15,000. Of cancer patients who had post-college education, 13.9% used questionable cancer treatments compared with only five percent of those who did not complete high school. Likely simply reiterating the issue of affluence and education, Caucasians utilized questionable treatments at almost twice the rate of non-Caucasians (9.5% for Caucasians, 7.3% for blacks, and 2.3% for Hispanics).

CHARACTERISTICS OF PURVEYORS

In the most comprehensively available study about the practitioners of questionable cancer treatments, Cassileth¹ determined that 60% of the providers of such treatments were medical physicians. Of these, 83% received medical degrees in the United States. Of the physicians, 18% were Board certified in internal medicine, family practice, surgery, neurosurgery, urology or psychiatry. The remaining 40% were also considered "professionals," that is, were chiropractors, osteopaths, naturopaths, homeopaths, or nutritionists. Undoubtedly, some in the latter categories are the products of poorly controlled "diploma mills," but this appeared to represent a relatively small number.

PERCEPTIONS OF PATIENTS V PHYSICIANS REGARDING THE TREATING PHYSICIAN'S ROLE IN QUESTIONABLE TREATMENT USE

Family and Patient Perceptions. One of the startling conclusions of the American Cancer Society national sur-

From the University of Minnesota School of Medicine, St Paul, MN.
Address correspondence to Dr Lerner, Clinical Professor of Medicine, University of Minnesota, 310 North Smith Avenue, Suite 460, St Paul, MN 55102.

TABLE I. Questionable Cancer Treatments and Promoters of Highest Concern to the American Cancer Society

Antineoplastons
Cancell
Committee for Freedom of Choice in Medicine, Inc.
Contreras method
Greek Cancer Cure of Hariton Alivizatos
Immuno-augmentative therapy of Lawrence Burton, PhD, Bahamas
Laetrile
Livingston-Wheeler therapy
Macrobiotic diets for the treatment of cancer
National Health Federation
O. Carl Simonton, MD
Questionable cancer practices in Tijuana and other Mexican border clinics
Questionable immune modulation in the treatment of cancer
Revici method

Source: American Cancer Society

vey⁴ of patients was the overwhelming patient perception that the use of questionable cancer treatments was largely facilitated by physicians. Patients and their families reported that overall 35% of the time the questionable cancer treatment method had been "recommended" by the patient's primary physician, and that it had been "approved" another 15% of the time. They reported that in only 35% of cases were the questionable treatment methods used unbeknownst to the physician, and only two percent over the stated "objection" of the physician. On the basis of these responses on the part of patients and their families, the surveying firm carrying out the American Cancer Society study concluded "physicians caring for cancer patients regulate the use of unproven cancer treatments more than does any other agent."² Moreover, patients and their families stated that in 31% of the cases they were originally introduced to the questionable treatment method by their primary physician. As such, physicians were alleged to be the leading source of the initial information about these methods.

Physician Perceptions. The public contention that physicians were the prime source of information about questionable cancer treatment methods and that the primary physician usually recommended or at least approved of these treatment methods was so startling that the American Cancer Society commissioned a second national survey to evaluate physicians' perceptions. Although the physician survey⁴ was distinctly smaller than the patient survey (104 physicians interviewed), the perception of the physicians

TABLE II. Questionable Cancer Treatments and Promoters of High Concern to the American Cancer Society

Dimethyl sulfoxide (DMSO)
Gerson method
Hoxsey method
International Association of Cancer Victors and Friends, Inc.
Iscador
Live cell therapy
The metabolic cancer therapy of Harold W. Manner, PhD
Hans Nieper, MD
Nutritional and metabolic cancer therapy of William D. Kelley
The promotion of hydrogen peroxide, germanium, and ozone therapy in the treatment of cancer
Psychic surgery

Source: American Cancer Society.

was uniformly at sharp variance from that of the patients. Physicians contended that when they were aware their patients used questionable cancer treatments, they actively tried to discourage that use in 64% of cases. Moreover, physicians asserted that they "recommended" treatment in only two percent of cases, but that ultimately they "went along with" the questionable treatment 37% of the time.

The Issue of Physician Responsibility. The federal government has a clear responsibility to protect patients from questionable treatments for all forms of disease. The Food and Drug Administration (FDA) is the agency charged with enforcing the Federal Food, Drug and Cosmetic Act, which provides that all treatments must be conclusively proven to be safe and effective for their stated purpose before they can be legally marketed in the United States. Senator Edward Kennedy defined this responsibility in his remarks during the 1977 Senate Hearings about Laetrile: "The role of the Food and Drug Administration is to guarantee that the available drug therapies are the best and most effective that science can devise. Their role is to protect both the patient and his family from remedies that are neither safe nor effective. The elimination of useless treatments is a valid federal role."¹¹

The responsibility of individual physicians in this area, however, is much less well defined. It has been argued that physicians should adopt a position of caveat emptor and, moreover, that according to the "forbidden fruit" argument, physician opposition to questionable treatments might make them even more attractive in the public eye.¹² In contrast, in my view, physicians have always had a major responsibility in serving as their patients' advocates, and in the complex modern world of slick marketing techniques the need for their doing so is even greater. Patients have a right to look to their doctors for counsel in health matters of all sorts, but certainly regarding unscientific, unsafe, worthless medical practices.

GUIDELINES FOR AN EFFECTIVE PHYSICIAN ROLE

Avoid Patient Abandonment. The patient who is either overtly or implicitly abandoned by his physician is effectively driven to the questionable practitioner. As the most successful cancer quack promoter of the 1950s put it, "Cancer victims come to us because they are unwilling to accept as final a death sentence handed them by their own doctors."¹³ Even when a physician must honestly concede that there is no longer any effective treatment option remaining for a malignancy or any other disease, the fundamental responsibility persists for caring for that patient, steadfastly attempting to ameliorate physical and emotional suffering. Anything less amounts to abandonment in varying degrees and encourages the patient to seek an "alternative" therapist.

A Strategy of Preemptive Discussion. If patients report that they do not discuss the option of questionable cancer treatments at all with their physicians 35% of the time and if experience indicates that patients frequently originally raise the issue of questionable treatments after they have already become committed to them, it would seem that an alternative strategy for physician/patient dialogues on this subject is indicated. One could argue that the physician should take the initiative in this area and introduce the subject early on in the discussion of the cancer problem and its ramifications. Certainly the physician is in a position to identify patients who should be considered at high risk for

trying questionable cancer treatments, particularly those of higher educational status and economic means who apparently are more willing to be adventurous and take risks. An appropriate opening for such a preemptive strategy would be: "In addition to the proven treatment modalities which we have discussed, you will very likely be approached by well-meaning persons with recommendations to try a variety of unscientific or unproven 'alternative treatments.' I can appreciate how attractive some of these ideas may sound, particularly in the context of the realities of dealing with a cancer situation, and I want you to know that I am available to discuss such proposals with you and to try to help you make a good decision."

Such a strategy has several obvious advantages. In the first place, it establishes that this body of information is as acceptable for discussion between doctor and patient as all other issues relating to the cancer. The patient clearly need not be embarrassed or hesitant to raise the subject. Secondly, the invitation is extended to learn about such treatments with the help of a scientific professional before the patient has become committed to a questionable treatment practice. Many of the questionable treatment practices are promoted with an intense evangelistic zeal, and, clearly, highly intelligent, well-educated individuals afflicted with the awesome disease, cancer, are exceedingly vulnerable to such emotional pitches. Hopefully, preempting the issue will enable the physician to avoid the later confrontation with an absolutely committed patient which frequently deteriorates into an unproductive and even hostile debate. The art in these dialogues is to disapprove emphatically, but calmly with the method without ever disapproving of the patient. Ultimately, it seems likely that inviting discussion about questionable treatment methods early on should improve the prospects of successfully guiding patients to adherence to proven scientific treatments.

A Source of Reliable Information. In all areas of medical practice, patients look to their physicians as their major source of medical information, and surely physicians recognize that their role as patient educators is a major aspect of medical practice. Studies indicate, however, that physicians consistently underestimate their patients' desire for complete medical information and they consistently overestimate the amount of time that they devote to the educational enterprise.¹⁴ In the area of questionable cancer treatments, since the alternative sources of information available to patients usually represent self-interested promoters, evangelistic friends, and pure hearsay, the need for the physician as patient educator is especially critical. Unfortunately, it would appear that physicians have tended to be relatively little interested in this issue and certainly generally ill-informed. While one recognizes that all doctors clearly cannot be expert in all areas, physicians are, by virtue of their training, capable of providing invaluable information that can make the difference between a patient selecting or rejecting questionable cancer treatments.

Physicians have been traditionally well schooled in understanding "the rules of the game" for establishing safety and efficacy, and in their continued educational process are constantly exposed to treatments which are being critically evaluated. Consequently, physicians should have good insight into the critical distinctions between FDA-approved treatments, genuine investigational treatments, and questionable treatments. Patients, however, frequently find these distinctions very confusing, especially when questionable proponents employ their slick, seductive arguments. A

physician should be able to explain clearly and briefly how a treatment modality passes the tests of safety and efficacy in controlled trials, in a reproducible fashion, and is exposed to peer review, so that it can meet FDA acceptance. Similarly, a physician can clarify that an investigational therapeutic, having demonstrated safety and efficacy in animal models, is currently involved in the process of controlled human trials. In contrast, a questionable method is defined as one which has either never been studied at all in a bona fide experimental setting or one which has failed that scientific study. In addition, especially to counter the common, paranoid argument of the questionable-methods promoters that the establishment is purposely withholding approval of their treatments, it is important that the physician point out that the rules of the game require any promoter to prove the safety and efficacy of his treatment, not for the "medical establishment" to disprove that.

Similarly, physicians can be expected to have good insight into the fallacies of traditional questionable treatment promotion techniques, but even sophisticated patients will frequently be confused by these. It would be worthwhile to review several of the more important such issues: *Testimonials*, usually delivered by fervent true believers, have been the bedrock of questionable method promotions for centuries. Physicians, by their training, recognize that these are nothing more than anecdotes, which may be interesting and may even merit additional evaluation, but that in their own right they hold no scientific substance. The rules of the game require objective measurement of benefit in a treated group as compared to a non-treated group and that this be reproducible before the treatment can be accepted as valuable. That an intense individual may fervently proclaim that something is so, no matter the depth of his belief, does not make it so.

Scientific medicine recognizes the value, but also the substantial limitations of the *placebo effect*. Especially in the area of advanced cancer, the argument has frequently been proposed that treatments solely producing placebo effect should be accepted as standard therapies. For example, in a state legislative hearing regarding the legalization of Laetrile, "One New York state legislator put it this way: 'When you drive your car out of a car wash, doesn't it seem to run better?' 'Maybe,' replied the FDA official, 'but my car would really run better if it had an engine job. And if anyone tells you a wash will improve your car's performance, he is committing fraud.'"¹⁵

Exclusively subjective responses frequently are the consequence of the placebo effect, but surely there are treatments which will produce improved energy, appetite and well-being of more durability than most placebo effects. Scientific medicine has just begun the very arduous enterprise of trying to evaluate these kinds of "quality of life" responses when they lack objective confirmation. It seems reasonable that we will become more sophisticated in evaluating these responses and that treatments will be approved solely for this purpose. Inasmuch as the questionable treatment promoters, however, make no scientific effort to evaluate treatment responses, their description of exclusive subjective responses is obviously highly suspect. This is especially true because the field of questionable cancer practices is replete with instances of patients who were allegedly feeling better while their diseases were unequivocally progressing to their death.

Inappropriate diagnoses have been a substantial problem in questionable treatment promotions in the past and

continue to some degree to be so to this day. Patients have been treated for "precancer"¹⁶ as defined by various symptom complexes of common ailments like abdominal gas, blurry vision, or morning malaise. Certainly, treatment of such "disease" will inevitably be associated with a very high success rate and obviously have no validity. Questionable cancer practitioners differ considerably in their requirement for the establishment of a malignant disease, but clearly many will treat merely on the basis of the patient's concern that he may have cancer, and many patients are treated on the basis of cancer diagnostic tests that have absolutely no scientific validity.

A major source of confusion for patients has been the situation of a patient measurably improving in the context of a questionable cancer treatment, but also having received *coincidental conventional treatment*. Since the scientific treatment has frequently been associated with adverse effects and the patient becomes a "convert" to the questionable treatment, the patient is apt to describe all success to the questionable treatment and all trouble to the conventional treatment. Many of the most striking "successes" of questionable cancer treatments clearly were the result of preceding or coexistent conventional treatments. For example, the individual who received federal court approval to import his personal supply of Laetrile as a lifesaving drug had unquestionably been cured of his early rectal carcinoma by local surgery before ever beginning Laetrile.¹⁵

Specific Questionable Methods. One expects physicians to be generally knowledgeable on the above issues, but surely each physician can't be expected to know the vagaries of the specific questionable treatment promotions. The history of these treatments is frequently convoluted, the methodology often bizarre and out of the context of scientific medicine, and the alleged results presented as testimonials and hearsay rather than scientific data. Physicians are not expected to be expert in all areas of medicine, but they can be expected to serve as a source of medical information when asked about a new or novel test or treatment. Physicians know how to obtain such information for their patients or at least how to direct their patients to obtaining the information for themselves. In the area of questionable treatment methods, however, it appears that physicians do not recognize ready sources of information and all too often have simply expressed disapproval without an interest in obtaining information. The American Cancer Society, for example, keeps exhaustive files on a great variety of questionable treatment methods and has position papers on a large number of these, but the Society receives relatively few inquiries from medical professionals. In addition to literature regarding the treatment methods, the Society is also in a position to direct inquiring physicians to experts, locally or nationally, who are available to discuss a particular treatment with them or their patients. A single phone call to the physician's local division headquarters of the American Cancer Society or to the national office of the Society should be adequate to provide the necessary information on a great variety of questionable treatment promotions. In addition, the American Society of Clinical Oncology, the FDA, the National Cancer Institute, and the US Pharmacopeia may be additional sources for specific kinds of information.

Especially recognizing the extraordinarily sophisticated and seductive arguments of questionable method purveyors, the primary physician would be well advised not to accept the mantle of expert on a given questionable

treatment method unless, in fact, he is. Debates with patient "true believers" or the promoters themselves have a major risk of deteriorating into adversarial confrontations that are at high risk for producing a "lose/lose" resolution. A physician serves his patient far better to offer to obtain objective information about the method, to help evaluate that information, and, without ever condoning the treatment method, by making it clear that he will continue to serve the patient regardless of the treatment option that the patient pursues.

ADDRESSING THEMES OF QUESTIONABLE TREATMENT PROMOTIONS IN THE CONTEXT OF SCIENTIFIC MEDICINE

Particularly in the last two decades, patients' attitudes toward their health care have evolved very considerably, and questionable treatment practitioners have been especially astute in reacting to this. The traditional role of the doctor as the activist treater and the patient as a passive recipient, dutifully taking his medication, is *passee*. Patients want to be proactive in attending to their health needs, consistent with the contemporary, "do-it-yourself" attitude in many other walks of life. In addition, patients are much less apt now to be satisfied with being considered a faulty organ system, a failed heart, a breast cancer, a stomach ulcer; rather, they want to be considered a total being with various ailments a component of their physical and spiritual totality. Questionable treatment promoters have been extraordinarily effective in selling their concept of "holistic" health care and providing their patients with a great variety of activist approaches to their health protection and disease treatment. Traditional medicine has been much slower to react to these changes and has been put at a disadvantage in these areas.

Clearly, the increasing status of the primary care-giver as a treater of the whole patient is a major step in the right direction. Specialist medicine still too often focuses on a specific diseased organ or system rather than the whole patient. All physicians, generalists and specialists, need to be alert to this issue, working always to be sensitive to the patient's overall physical and emotional well-being.

The error in the questionable treatment purveyors' promotion of specific nutritional schemes, exercise programs, and "attitude adjustments" is not in addressing these issues, but in the specifics of their methodology and particularly in the promise of their value. Surely, scientific physicians have been remiss in underemphasizing good nutrition, good physical conditioning, and good mental attitudes. We need to encourage patients to have an adequate caloric intake and protein intake in the treatment of cancer, as well as in all other walks of life. In doing so, although, it is important that we define what is inadequate nutrition and make clear to patients that good nutrition will not fix cancer, but will help maintain their ability independently to resist the cancer and to tolerate the frequently arduous legitimate anticancer treatments. Similarly, physical conditioning is important for everyone, surely including patients afflicted with cancer. Good conditioning enhances their general well-being and their ability to tolerate treatments. The value in having a "positive attitude" is not that it will prevent cancer or diminish an existing cancer, for there is no evidence to support this.¹⁷ The value lies in the fact that patients who are upbeat and optimistic about their situation are clearly happier individuals who are more comfortable for their family, friends, and medical therapists to interact with so that they do not become socially

isolated. It would seem that such positive people are far more likely to be able to sustain the rigors of their scientific anticancer treatment. Good nutrition, good conditioning, and a good attitude are all clearly good things which we as physicians should actively promote, but we must also be honest enough to make it clear to our patients that they will not stop cancer unless we also have effective treatment.

One apparent value of many forms of questionable cancer treatments is that they represent forms of group therapy. Patients in these settings are treated in groups, share mutual experiences, and oftentimes participate in their "self-help" endeavors in group ways. Although for some patients the cancer experience is a very private matter, for many others it is dramatically more tolerable when shared with others with similar problems. Supportive group meetings are available in the context of scientific anticancer treatment as well, but have probably been underused. Each patient should be offered the opportunity early on in a discussion of his cancer problem of participating in a support group, and it is imperative that treating physicians are knowledgeable about the groups available in their area. Again, the American Cancer Society is a sponsor of many such groups, and can be a valuable source of information for those and others in the community. Some patients will require a more intensive, more personal therapeutic experience to deal with the emotional aspects of living with cancer, so that the primary physician must identify consultants in this area as in all others.

CONCLUSIONS

Like it or not, quality medical care of the cancer patient in the 1990s requires that the treating physician deal with the issue of questionable cancer treatment practices. Most physicians probably don't like it because they find the entire subject of "quackery" distasteful and because they are not especially knowledgeable about it. Nevertheless, with nine percent of their patients indulging in these practices nationwide, oftentimes early on in the diagnosis of their disease, not infrequently to the exclusion of scientific anticancer treatment, the issue must be addressed. That such a significant percentage of questionable treatment practitioners are medical physicians is a disgrace and clearly speaks to the need for better educational efforts at the medical school and post-graduate level, as well as for better enforcement efforts by our regulatory bodies. That such a high percentage of patients profess that their physicians introduce them to questionable treatment methods and encourage or condone those methods, while physicians clearly feel that they are attempting to discour-

age such treatments, speaks to a failure of doctor/patient communication. One strategy to try to address this problem is for the physician to introduce the subject of questionable treatment methods early in the discussion of the ramifications of the cancer situation. This must be presented as a topic as available for discussion as any other, with the physician being able to draw a clear distinction between approved treatments, investigational treatments, and questionable treatments, and with the physician being conversant in the many fallacies of questionable treatment promotions. In addition, physicians of the 1990s need to be thoroughly sensitive to the desire of their patients to be treated as whole persons rather than specific disease entities and as persons who wish actively to be involved in their health care maintenance or their treatment. These are legitimate expectations that we can encourage and develop without in any way sharing in the false promise of the quack.

REFERENCES

1. Cassileth BR, Lusk EJ, Strouse TB, et al: Contemporary unorthodox treatments in cancer medicine: a study of patients, treatments, and practitioners. *Ann Intern Med* 1984; 101:105-112.
2. Shapiro LJ and Associates: *The prevalence of unproven cancer treatments in the United States*. Report to the committee on methods of unproven cancer management of the American Cancer Society 1989.
3. Cassileth BR, Brown H: Unorthodox cancer medicine. *CA Can J Clin* 1988; 38:176-185.
4. Lerner IJ, Kennedy BJ: The prevalence of questionable methods of cancer treatments in the United States. *CA Can J Clin* 1992; 42:181-191.
5. Goldstein J, Chao C, Valentine E, et al: A survey of patients' use of unproven cancer treatments in a radiation oncology department. *J Psychosoc Oncol* 1991; 9(3):59-66.
6. Faw C, Ballentine R, Ballentine L, et al: Unproven cancer remedies: a survey of use in pediatric outpatients. *JAMA* 1977; 238:1536-1538.
7. Eidinger RN, Schapira DV: Cancer patients' insight into their treatment, prognosis and unconventional therapies. *Cancer* 1984; 53:2736-2740.
8. Copeland DR, Silberberg Y, Pfefferbaum B: Attitudes and practices of families of children in treatment for cancer: a cross-cultural study. *Am J Pediatr Hematol Oncol* 1983; 5:65-71.
9. Mooney K: Unproven cancer treatment usage in cancer patients who have received conventional therapy. *Oncology Nursing Forum* 1987; (supp2): 112(abst124A).
10. Newell SM: An investigation into the utility of the modified health belief model in predicting treatment compliance for advanced adult cancer patients in hospital outpatient clinics. *Dissertations Abstract International* 1985; 45:3201-3208.
11. Monaco GP: The primary care physician: the first line of defense in the battle against health fraud. *Medical Times* 1986; 114:43-48.
12. Crile G: Legalization of laetrile—a suggestion. *N Engl J Med* 1976; 295: 116.
13. Hoxsey H, Janssen WF: Cancer quackery: the past in the present. *Semin Oncology* 1979; 6:535.
14. Waitzkin H: Information giving in medical care. *J Health Soc Behav* 1985; 26:81-101.
15. Laetrile—The political success of a scientific failure. *Consumer Reports* 1977; 42:444-447.
16. Kelly WD: *One Answer to Cancer*. Kelly Research Foundation 1969.
17. Cassileth BR, Lusk EJ, Miller DS, et al: Psychosocial correlates of survival in advanced malignant disease? *N Engl J Med* 1985; 312:1551-1555.

Allergy-related quackery

WILLIAM T. JARVIS, PhD

Quack: "a pretender to medical skill." (Websters New Collegiate Dictionary); "One who fraudulently misrepresents his ability and experience in the diagnosis and treatment of disease or the effects to be achieved by the treatment he offers." (Dorlands Illustrated Medical Dictionary)

From the Department of Public Health and Preventative Medicine, Loma Linda University School of Medicine, Loma Linda, CA.
Address correspondence to Dr Jarvis, PO Box 1276, Loma Linda, CA 92354.

Standard reference definitions of quackery wrongly focus on pretense as the quack's chief characteristic. Although it is true that quacks are always incompetent for the job at hand, pretender implies that all quacks are impostors, disregarding the fact that many quacks are physicians who have ventured outside of their fields, or abandoned the scientific rigor and ethics of their professions. Other definitions wrongly limit quackery to fraud. This overlooks the

most dangerous of all quacks who are true believers whose zealotry knows no reasonable limits. Sincerity may make quackery more socially tolerable, but it only serves to make it more dangerous.

A Congressional committee investigating the problem defined quackery as the practices and pretensions of a quack; quack was defined as "Anyone who *promotes* (emphasis added) medical schemes or remedies known to be false, or which are unproven, for a profit."¹ The Committee rightly focused upon the word *promotes* as the operative term in its definition. To promote is "to contribute to the growth and prosperity of; to present for public acceptance through advertising and publicity."² Promotionalism is the essence of quackery because the term is derived from quacksalver which means literally to "quack like a duck about (one's) salves and remedies."³ Advertising represents recognizable commercial communications clearly designed to sell something. Advertisements have limited First Amendment protection in that they may not be false or misleading. Although quacks often violate the rules against false and misleading advertising, at least the public is more likely to be on its guard to a degree when dealing with recognizable advertising. Publicity includes communications that which enjoy the right to free speech. The public is at a major disadvantage when faced with false and unproven remedies in books, magazine and newspaper articles, lectures, audio and video cassettes, talk show appearances, and other such activities. The financial interest of promoters is often disguised in such communications. This type of "hidden advertising" is the most problematic because it enjoys greater First Amendment protection.

CONFUSION ABOUT ALLERGIES

Quackery thrives within an atmosphere of confusion. Allergies lend themselves to exploitation because they can be real or imagined, their true nature is poorly understood by the public and even by some health professionals, and both patients and practitioners may benefit from their misdiagnosis. Inconsistency in the terms used by physicians to refer to adverse reactions furthers the confusion surrounding this topic. Although what is usually termed allergies in non-food-related reactions manifest established immunological characteristics, food-related "allergies" are often confused with "intolerances," (eg, lactose intolerance), "idiosyncracies" (ie, unique personal reaction to specific foods), or "sensitivities." To avoid misdefinition, Bock prefers "sensitivity" to describe immunological mediated response,⁴ while Truswell believes "food allergy" should be confined to immunological reactions.⁵ Recognized experts agree that immunological and nonimmunological responses must be distinguished to clarify the matter.

ALLERGIES AND POP CULTURE

The public believes that food allergies are more widespread than scientific evidence will support. In a random sample of 3,300 American Adults, 43% said they have some type of adverse reaction to foods, a reaction often ascribed to a food allergy.⁶ Dr Jordan Fink, chief allergist at the Medical College of Wisconsin, says that the actual incidence of true food allergy is about 2% of the population.⁷ Current media attention to toxic dump sites, mysterious polychlorinated biphenyl contamination, Vietnam veteran's allegations about agent-orange-related disorders has heightened public concern.

MISDIAGNOSIS

Faulty Diagnostic Tests. A substantial amount of allergy quackery is founded on invalid diagnostic testing. Clinical laboratory entrepreneurs have been quick to market dubious allergy tests, and cooperate with maverick practitioners. Advertising and publicity generated by the marketing of bogus allergy testing and treatment reinforces common myths. The American Academy of Allergy and Immunology commented on five controversial techniques used to diagnose allergies:

1. Cytotoxic testing (Bryan's Test). Observations are made of the effects on white cells when food derivatives are mixed with blood samples. Although the test appeals to logic, it fails by producing excessive false positives and false negatives.
2. Urine autoinjection (autogenous urine immunization)
3. Skin titration (Rinkel method).
4. Provocative and neutralization testing (subcutaneous).
5. Provocative testing (sublingual).⁸

Other invalid diagnostic tests include "applied kinesiology," a chiropractic method that tests muscular strength reactions to suspected allergens;⁹ radionics, which employs electronic devices alleged to measure "energy;"¹⁰ medical dowsing, which uses a pendulum or dowsing rods; and others.

Somatization. What passes as environmental illness is indistinguishable from common psychiatric disorders. Somatization explains why many patients readily accept their misdiagnoses. Somatists are likely to favor a diagnosis of chemical sensitivity because it permits them to blame factors outside of themselves for their uncomfortable lives. Society's tendency to view people with psychological problems as being inferior encourages the denial of psychiatric disorder. Stewart¹¹⁻¹⁴ found that about 60% of sufferers are amenable to treatment, but the others refuse to relinquish their diagnoses for self-serving reasons. The symptoms of fictitious allergy sufferers are indistinguishable from those in the past and present who have been misdiagnosed as having "neurasthenia," "reactive hypoglycemia," or "adrenal insufficiency." Contemporary diagnoses include "yeast infection" (candidiasis), "dental amalgam toxicity," "chronic fatigue syndrome," and "environmental illness."

Research Findings. Objective evidence of food hypersensitivity was sought by the use of exclusion diets and provocation tests in 23 patients who attributed a wide variety of symptoms to food allergy. Hypersensitivity to ingested substances was confirmed in four, each of whom presented with typical atopic symptoms. None of these had psychological symptoms, but a high incidence of psychiatric disorder was found in patients whose belief that they had a food allergy could not be confirmed.¹⁵ Black et al evaluated 26 subjects who had been diagnosed with environmental illness. They described the subjects as having a strong interest in their diagnosis, generally satisfied with their clinical ecologists, and dissatisfied with regular medical approaches. They found that 15 (65%) met criteria for a current or past mood, anxiety, or somatoform disorder, compared with 13 (28%) of 46 age and gender matched controls. They concluded that patients receiving this diagnosis may have one or more commonly recognized psychiatric disorders that could explain some or all of their symptoms.¹⁶ Simon et al studied 37 symptomatic plastics workers who experienced a chemical exposure. They found that 13 subjects who developed environmental illness scored higher on all measures of somatization and psychopathology than the others. They concluded that psychological vulnerability strongly influences chemical sensitivity after exposure.¹⁷ Brodsky described eight clinical ecology patients as sharing

common features: (1) their claim of injury by toxic elements in the work environment rarely began with a specific event of exposure; (2) no physical evidence of injury was found by established diagnostic methods; (3) most have a history of overt psychiatric symptoms; (4) all but one are women; (5) all too frequently they have been seen by the same network of physicians who subscribe to clinical ecology; and (6) their self-perception and diagnosis of "allergic" to most substances have become an organizing principle in their lives, central to their identity and life-style.¹⁸

Conversion-V. Patients who gain from their illnesses are sometimes identifiable by the Minnesota Multiphasic Personality Inventory by what is termed the "Conversion V profile" (ie, high in hypochondriasis, low in depression, and high in hysteria). This pattern is descriptive of persons who somatize emotional problems and are resistant to psychological intervention or interpretation of their symptoms.¹⁹

PSYCHOLOGICAL INFLUENCES

Pediatric allergist and researcher, Alan Bock, points out that careful studies have shown that about 60% of children with histories of adverse reactions to foods cannot be confirmed when a double-blind food challenge is administered. His work strongly suggests that the reactions are based on social factors, belief or operant conditioning.

Power of the Imagination. The discrepancy between real and imagined food allergies is in part due to a failure to differentiate between true allergies and adverse reactions due to negative beliefs about certain foods or operant conditioning. A committed vegetarian, who believed herself to be allergic to flesh-foods, collapsed at a church potluck after tasting what she thought was meat. When told that she had not eaten meat but a new vegetarian meat-analog, although somewhat embarrassed, she recovered almost immediately. We may find it easier to empathize if we imagined ourselves in a cultural setting in which we were served repulsive foods (eg, insect larvae [dietary fare of Australian aborigines], duck brains (a Chinese delicacy), or dog meat (an American Indian ceremonial food)). The author recalls that a former geography professor once said that the first question she was asked upon stepping off an airplane in India during the 1940s was "is it true that Americans eat the filthy swine?" This incredulous question came from a Hindu who, as a follower of traditional ayurvedic medicine, thought it healthful to use his own urine as mouthwash!

Operant conditioning can also cause adverse reactions to foods. A woman who previously liked caramel has reacted adversely to its smell since its odor and her ill-feelings became linked in her mind because her mother was cooking caramel while she was sick at home as a child. Although she is aware that her reaction is operant conditioning, she has been unable to overcome the response for 45 years. Psychological influences upon adverse food reactions should not be underestimated.

Practitioner Influence. Anxiety and depression are common psychiatric symptoms. The strong belief of a practitioner who convinces a patient that he or she has located the problem and is specifically treating it can create an enthusiasm that will itself relieve either anxiety or depression.

QUESTIONABLE PRACTITIONERS

Questionable practitioners appear more often to be guilty of bad science than malice. Clinicians unskilled in scientific methodology, and the pitfalls of uncontrolled

clinical experiences, can easily fall into the "seeing is believing" fallacy. Patients may manifest any number of symptoms known to be associated with conversion illnesses. Patients exposed only to single-blind testing can react by interpreting the expectations of practitioners administering the suspected noxious agents. From a methodological perspective, the only protocol that can ensure valid results are cross-over challenge tests in which the patient, practitioner administering the treatment, and the practitioner evaluating the outcomes are all blinded. Sound clinical research methodology has been outlined in the literature.²⁰

Several practice guilds have bound together into pressure groups to advance their practices both politically and economically. Like folk medicine practitioners who "merely specialize in what everyone knows; with no significant difference in conception of illness separating them from their patients,"²¹ allergy quacks may be both victims as well as victimizers. Practitioners who hold misbeliefs about allergies and do not use proper scientific methods can easily be fooled by a combination of their expectations and their patients' subjective responses.

The Shot Doctors. Although allergy shots can be a legitimate therapeutic approach, their use sometimes takes the form of abuse. In 1988, *Consumer's Union* warned the public about doctors who send patients' blood samples through the mail for allergy diagnoses, and then treat alleged allergies with shots instead of recommending suitable medications or referring to qualified allergy specialists. The authors found significant discrepancies between samples sent to different labs offering similar services.²²

Clinical Ecology. Clinical ecology is an unrecognized subspecialty of practitioners who claim that a broad range of common physical and psychological disorders can be triggered in susceptible persons by ongoing low-level exposure to chemicals or foods. Patients are said to be suffering from "environmental illness," "brain allergy," "food addiction," "ingestant intolerance," or are allergic to "the 20th century," "everything modern," or simply everything in "total allergy syndrome."

The idea of clinical ecology was originated by a physician, Theron Randolph, who diagnosed the condition in himself. Randolph married one of his patients. Both believed that they became ill if they ate ordinary food. The couple won a case brought against them by the Internal Revenue Service (IRS) for deducting \$3,000 of their \$6,000 food bill for the year (1971) which they spent on "organically grown" foods to avoid adverse reactions.²³

In 1981, the California Medical Association (CMA) adopted the position that clinical ecology does not constitute a valid medical discipline and that scientific and clinical evidence to support the diagnosis of "environmental illness" and "cerebral allergy" or the concept of massive environmental allergy is lacking. As a result of requests from clinical ecologists to justify their claims, the CMA appointed a task force in 1984 to review clinical ecology. The task force concluded that (1) there is no convincing evidence that supports the hypotheses on which clinical ecology is based; (2) clinical ecologists have not identified specific, recognizable diseases caused by exposure to low level environmental stressors; (3) methods to diagnose and treat such unidentified conditions have not been shown to be effective; (4) the practice of clinical ecology can be considered experimental only when its practitioners adhere to scientifically sound research protocols and inform their patients about the experimental nature of their practice.²⁴

In 1986, the American Academy of Allergy and Immunology concluded that "the diagnostic and therapeutic principles used to support the concept of clinical ecology indicates that it is an unproven and experimental methodology."²⁵ In 1989, the American College of Physicians also issued a position paper against clinical ecology.²⁶

Scientology. Scientology which sells itself as a "alternative" approach to clinical psychology or psychiatry, has embraced the notion of environmental illness. Scientology operates HealthMed, some of whose physicians are clinical ecologists, and markets "Purification Rundown" (PR), a detoxification program created by Scientology's charismatic founder L. Ron Hubbard. Scientology's reputation as a cult (ie, "a system for the cure of disease based upon dogma set forth by its promulgator")² is supported by the fact that its practitioners advocate Hubbard's remedy based primarily on his status as guru. On the basis of the idea that body loads of environmental poisons are at the root of many behavioral problems, PR claims to detoxify the body by megadoses of niacin for dilating blood vessels (ie, the niacin blush), and sweating out poisons through steam baths and exercise. The method was popularized in a book, *Diet for a Poisoned Planet*, by David Steinman.²⁷ The FDA declared that Steinman's book misrepresented FDA data, and pointed out the invalidity and potential hazards of the PR in a press release.²⁸

BENEFITS AND HARMS

Some may argue that there are positive effects to misdiagnosing psychological problems as due to food allergies or environmental toxins. Having an outside force to focus their frustrations upon could improve the child-parent relationship. A "hyperactive" child, whose parents come to believe that his or her troubles are due to dietary factors rather than behavior patterns, is able to get some relief as parents cast the blame away from the child to nasty old sugar or something of the sort. Likewise, parents may be able to assuage their guilt of having failed in their childrearing by scapegoating bad foods. However, such theoretical benefits must be balanced against harms which might accrue. For instance, diagnosing non-existent food allergies in a patient can have a major impact on his or her lifestyle and social interactions. Children may have to forego important experiences needed for normal social development such as going to camp, pajama parties, sleeping over with friends, going to birthday parties, and so forth, out of a parent's fear that they will ingest a forbidden food. Causing children to feel physically impaired can teach hypochondria and weaken self concept.

Being able to blame factors outside of themselves for their internal or relationship problems appeals to many people. A number of parents found comfort in Feingold's book *Why Your Child is Hyperactive*,²⁹ and groups organized around his theories. Studies failed to confirm Feingold's hypothesis, but many became believers based on their own subjective experiences and continue the movement to this day. Indirect harm can occur because Feingold groups tend to attract purveyors of nutrition quackery. We have seen raw milk, bee pollen, questionable herbs, megavitamins, and other potentially hazardous products promoted in lectures before such gatherings. Apparently, the alienation from scientific medicine and nutrition Feingold groups feel drives them to "experts" who will support their beliefs.

A Dramatic Case of Harm. Most misdiagnoses involve false positives in which patients are told that they have

allergies which do not exist, but the opposite has also occurred. Real food allergies can be serious, even life-threatening (eg, sulfite sensitivity). Misdiagnosis of a patient can needlessly prolong suffering, but failing to diagnose a real allergy can lead to serious consequences. An unusual case in which patients were told that they did not have an allergy when in fact they did, resulted in a near-fatal episode. The incident involved Canadian physician, Irvine Allen Korman, a clinical ecologist. A mother, herself a dentist, brought her two children to Korman for treatment of allergy problems both had experienced from birth. Her boy had become worse since starting school. The children were tested, the boy more so than the girl. Two unproved tests were used. The first involved the sublingual application of a solution (ie, the sublingual provocative test) followed by ten-minutes of observation for unusual behavior. The second test employed "applied kinesiology," a method in which the patient holds a closed glass container of a solution in one hand while the examiner tests the strength of the opposite abducted arm. The mother did not understand the second test and questioned Korman about the reliability and predictability of the procedure for assessing peanut sensitivity. Korman told her that he had absolute confidence and assured her that it was all right for her to feed the children peanut butter. The mother purchased some organically grown peanut butter and gave each child a tiny amount on a piece of bread. According to the report:

A dramatic scene followed. Both children collapsed. The girl was terribly white-faced, regained consciousness, was given medication, vomited, developed huge hives, but continued to breathe. The boy kept struggling, could not open his eyes, was gasping for breath, was blue and choking. An ambulance took the family to the hospital where the children were given adrenalin and within a few hours were fine again, but naturally somewhat shaken.

Dr Korman was given a recorded reprimand and had his license suspended for 60 days, with an additional 12-month suspension if he failed to complete the McMaster Physician Review Program with special attention to the areas of immunology, allergy, and nutrition.³⁰

Korman's license was revoked in 1990 for professional misconduct and incompetence. Korman's actions included testing a patient for allergies by swinging a quartz ball attached to a string, advising her to have her metal dental filings removed, and informing her that she was allergic to electricity. Several of Korman's patients testified in glowing terms of the doctor's success in treating their "environmental illnesses."³¹

PATIENTS: VICTIMS OR CO-CONSPIRATORS?

A Strange Kind of Patient Activism. Stewart notes that misdiagnosed somatization is unique in that patients organize into groups which oppose scientific study into their conditions rather than to encourage research.¹⁴ Some patients with misdiagnosed psychiatric problems appear to be more interested in fighting doctors who practice scientific medicine. In November 1990, a meeting of the American Academy of Allergy and Immunology was disrupted by clinical ecologists and their patients. According to a report by John C. Selner, MD:

We arrived at our workshop to find a number of patients confined to wheel chairs with oxygen masks in place, or wearing filters, who were identifiable as patients with so-called environmental illness. Approximately four hours into the workshop I was confronted by a

CBS radio news reporter who interrupted my presentation to ask if I was aware of a public demonstration in front of the hotel. The reporter indicated that he had been informed by environmental activists that a demonstration would take place. A clinical ecologist MD accompanied the demonstrators as they forced their way into the workshop. When asked to leave they refused and the ecologist demanded to have access to the platform. The workshop was recessed and the speakers dispersed to reconvene after the demonstrators had been evicted by the security personnel and local police.

It would appear that any programs which might address issues surrounding the effects of unproven and controversial methods of diagnosis and treatment may be targeted for such demonstrations in the future.

Irony might be found in the fact that the message the co-moderators of this workshop were attempting to highlight for psychiatrists and psychologists was the importance of taking patients very seriously who present without objective signs of disease, but with the so-called environmental illness scenario, and to recognize that many of these patients may be able to be helped. Furthermore, we were attempting to emphasize the importance of environmental chemicals in the induction of disease including psychological presentations.³²

This kind of patient behavior is probably what led Benjamin Franklin, founder of the US Postal service, including the Postal Inspectors office, to remark: "There are no greater liars than quacks, except for their patients."

Deep-Pocket Motivation. Some somatists use their maladies as coping devices for everyday living while others are litigants with a strong financial interest in being compensated for their pain and suffering in courts of law by a "deep-pocket" entity who they blame for their illnesses.

Harm to Society. In his book *Galileo's Revenge*,³³ Huber recently exposed the use of "junk science in the courtroom" in which cranks and quacks have been allowed to pollute the legal process by appearing as expert witnesses. Huber points out that the 1975 Federal Rules of Evidence opened the doors to the testimony of pseudoscientific "experts" by holding the previously recognized Frye rule obsolete which required that expert testimony be founded on theories, methods and procedures "generally accepted" as valid among other scientists in the same field. Huber described the work of Bertram W. Carnow, MD, of the University of Illinois School of Public Health. Huber said:

Carnow obtained his medical degree in 1951 but hasn't practiced medicine for 20 years. He registered for the board certification in internal medicine in 1957, 1958, 1960, 1961, 1962, 1963, and 1964, but withdrew twice and failed five times. He has since testified, under oath, that he sat for board certification in internal medicine only once. "I had completely forgotten" the other tries, Carnow explained in a 1983 UPI story. Today Carnow heads up Carnow, Conibear & Associates—the Conibear being Dr Shirley Conibear, Carnow's fourth wife (Third, testifies Carnow). The firm's best-known service is expert testimony.³⁴

Carnow's testimonial line extols the theory of clinical ecology. Huber writes that Carnow is backed up by Arthur C. Zahalsky, PhD, who teaches immunology to nursing undergraduates at Southern Illinois University, even though he never studied immunology in graduate school. The two helped plaintiffs obtain a \$49.2 million verdict against a chemical company in Missouri. With such large sums of

money at stake, and the inherent need on the part of somatists to deny psychiatric disorders, it is not surprising to discover patient organizations which lobby politically against the intrusion of critical, objective science into the problem of allergy misdiagnosis.

CONCLUSION

Allergy-related quackery is a serious problem with powerful psychological, social, and economic implications which favor its perpetuation. Health professionals, third party payers, lawmakers, regulatory agencies, the courts, and consumer groups must come together on the common ground of endorsing only sound scientific health care to curtail abuses and help patients find effective care.

REFERENCES

1. Pepper C: Quackery: A \$10 billion scandal. subcommittee on Health and Long-Term care of the Select Committee on Aging, United States House of Representatives, No.98-435, 1984.
2. Webster's New Collegiate Dictionary, Springfield, Mass: G&C Merriam Company, 1975.
3. Funk W. *Word Origins*. New York, Bell Publishing Company, 1950:111.
4. Bock SA: Food sensitivity. *Nutrition News* 1984; 43:(3):9-10.
5. Truswell AS: Food sensitivity. *Brit Med J* 1985; 291:951-5.
6. *Consumer Reports*, Feb, 1988, p98.
7. Thompson RC: *FDA Consumer*, June 1986, pp25-7.
8. American Academy of Allergy: Position statements—controversial techniques. *J Allergy Clin Immunol* 1981; 67:333-338.
9. Friedman MH, Weisburg J: Applied kinesiology—double-blind pilot study. *J Prosthet Dent* 1981; 45:321-323.
10. David TJ: The overworked and fraudulent diagnosis of food allergy and food intolerance in children. *J Royal Society Med* 1985; 78(suppl):21-31.
11. Stewart DE: Psychiatric assessment of patients with "20th-Century disease" (total allergy syndrome). *Canadian Med Assoc J* 1985; 133:1001-1006.
12. Stewart DE: Environmental hypersensitivity disorder, total allergy and 20th Century disease: a critical review. *Can Fam Physician* 1987; 33:405-410.
13. Stewart DE: The changing faces of somatization. *Psychosomatics* 1990; 31:153-158.
14. Stewart DE: Emotional disorders misdiagnosed as physical illness: environmental hypersensitivity, candidiasis hypersensitivity, and chronic fatigue syndrome. *International J Mental Health* 1990; 19:56-68.
15. Pearson DJ, Rix KJ, Bentley SJ: Food allergy: how much is in the mind? *The Lancet* 1983;(June 4):1259-1261.
16. Black DW, Rathe A, Goldstein RB: Environmental illness: a controlled study of 26 subjects with "20th Century disease." *JAMA* 1990; 264:3166-3170.
17. Simon GE, Katon WJ, Sparks PJ: Allergic to life: psychological factors in environmental illness. *Am J Psychiatry* 1990; 147:901-6.
18. Brodsky CM: "Allergic to everything": a medical subculture. *Psychosomatics* 1983; 24:731-42.
19. Johnson DD, Dorr KE, Swenson WM, et al: Alternative hypoglycemia. *JAMA* 1980; 1151-1155.
20. Metcalfe DD, Sampson HA: Workshop on experimental methodology for clinical studies of adverse reactions to foods and food additives. *J Allergy Clin Immunol* 1990; 86:421-442.
21. Friedson E: *Profession of Medicine*. New York: Harper & Row, 1970.
22. The Shot Doctors, *Consumer Reports*, 1988; (Feb):96-100.
23. Block J: Questioning medical deductions. *American Way*, March, 1984, p76.
24. Clinical ecology—a critical appraisal. *West J Med* 1986; 144:239-45.
25. Position statements: clinical ecology. *J Allergy Clin Immunol* 1986; 78:269-71.
26. American College of Physicians: Position paper: clinical ecology. *Annals of Internal Medicine* 1989; 111:168-178.
27. Steinman D: *Diet for a Poisoned Planet*. New York: Harmony Books, 1990.
28. Food and Drug Administration: "Poisoned planet"—A Diet for the Wrong Reasons, FDA Talk Paper, T90-48, October 15, 1990.
29. Feingold B: *Why Your Child is Hyperactive*. New York: Random House, 1975.
30. Discipline Committee, Report of Proceedings, The College of Physicians and Surgeons of Ontario, February, 1989, pp9-10.
31. Haliechuk R: MD who used quartz ball loses licence. *Toronto Star*, October 19, 1990.
32. Demonstrators disrupt allergy workshop, National Council Against Health Fraud Newsletter, 1991; 14:1:1-2.
33. Huber P: *Galileo's Revenge: Junk Science in the Courtroom*. New York: Basic Books, 1991.
34. Huber P: Spiel of fortune: how bad science wins big judgments. *Reason*, October, 1991, pp24-31.

Fertile field for fads and fraud

Questionable nutritional therapies

JOHANNA DWYER, DSC, RD

Questionable nutritional remedies are diagnostic tests or therapies used in the prevention, diagnosis or treatment of a disease, that, after review by qualified biomedical scientists and clinicians, are not recommended for clinical use.¹ Questionable dietary remedies differ from standard, well-accepted therapies in the quality and amount of evidence which exists for their claimed effects, safety, and use. Investigational and experimental therapies differ from questionable therapies. They are evaluated, after obtaining informed consent and review of the risks and benefits, using clinical trials or some other form of scientifically conducted investigation before clinical practice use. Questionable therapies are not subjected to such rigorous testing, risks and benefits are often not fully explained to patient users, and the questionable therapies have inadequate records of safety and effectiveness. Thus, they are not reasonable alternatives to either conventional or investigational nutritional therapies.

REASONS FOR CONCERN ABOUT QUESTIONABLE NUTRITIONAL REMEDIES

The use of questionable nutritional remedies sometimes diverts or delays patients from seeking more effective medical, nutritional, or psychological treatment for a curable disease, worsening it, making it more difficult to treat, and thereby causing needless illness. For example, one teenage patient with a benign tumor on her vocal cord refused to return for laser therapy, the conventional treatment for her condition. Her mother convinced her to interrupt her college studies, and to move home to Boston, where she spent over a year on a strict vegetarian regime prescribed by a lay healer who had touted the diet as curative for her condition. Only when she had lost the ability to speak altogether did she return for medical help which successfully cured her condition.

Some questionable therapies are hazardous. For example, questionable cancer remedies such as coffee enemas, diets that are devoid or very limited in animal foods, fasting, laetrile, or contaminated vaccines, have worsened the health and comfort of patients. The incidence of direct harm to patients is difficult to determine precisely, but there is good evidence that some of these cancer remedies are harmful.^{2,3} In addition, self-treatment of premenstrual syndrome with megadoses of vitamin B₆, another questionable remedy, has caused peripheral neuropathy in some

individuals who used it.⁴ Self dosing with megadoses of folic acid can mask the anemia that otherwise might signal the onset of vitamin B₁₂ deficiency. Physicians should rule out the possible presence of B₁₂ deficiency with the Schilling Test or by other means if there is reason to suspect problems.

Unfortunately, systematic reporting systems for toxic reactions from questionable nutritional therapies are presently inadequate. Neither health professionals nor users may be aware of problems until after they occur in so many people that their risks become obvious. For example, large doses of L-tryptophan were frequently used in the mid-1980s for questionable therapy of such disorders as sleeping problems, premenstrual syndrome, depression, stress, drug addiction, alcoholism, and for improving athletic performance. However, it was only after reports of over 1,000 cases of eosinophilia-myalgia syndrome and one death amassed that it became apparent that L-tryptophan from a contaminated product was causing the problem and the Food and Drug Administration recalled the product.⁵

Questionable nutritional remedies have risks, even when used with conventional therapies. Their side effects may interfere with treatment, cause malnutrition, other harm to physical health, or unnecessary emotional distress. For example, in a recent study of the questionable Livingstone-Wheeler cancer therapy, individuals who used both it and conventional therapies had lesser quality of life and unaltered survival when compared to those using conventional therapies alone.⁶

Another major reason for concern about questionable nutritional remedies is that they can detract from, rather than add to, quality of life, with no increase in disease-free periods or survival. Some unproved treatments interact or conflict with conventional treatments, decreasing effectiveness or increasing side effects. For example, patients on antihypertensive medications or insulin who embark on unsupervised use of very low calorie diets for weight control may develop side effects if medication doses are not decreased.

Nutritional status may be disrupted as a result of use of some of the questionable remedies. The financial costs of questionable therapies are often considerable. One recent estimate was that Americans spent over \$10 billion per year on questionable dietary practices of one sort or another.⁷

THE APPEAL OF QUESTIONABLE DIETARY REMEDIES

Today there is much public interest in nutritional means for promoting health and preventing disease and the mass media devotes attention to these issues. There is also much emphasis given to the importance of personal responsibility

From the Departments of Medicine and Community Health, Tufts University, Schools of Medicine and Nutrition, and the Frances Stern Nutrition Center, New England Medical Center Hospitals, Boston, MA 02111.

Address correspondence to Dr Dwyer, New England Medical Center, Box 783, 750 Washington St, Boston, MA 02111.

for one's own health and self help. Dietary measures are appealing because they seem to be more "natural," actively involve the patients, involve intimate contact with the body but are not invasive. Many individuals believe that diet caused their disease and that, ipso facto, there must be a dietary treatment for it.⁸ Patients often assume that advice for preventing disease also applies to its treatment. The self-help books and programs available on the market vary in their reliability, and further add to the confusion about what can be achieved by individual efforts.⁹ Patients often mistake the scientific jargon describing questionable nutritional remedies with scientifically demonstrated proof of effectiveness.¹⁰

The health-care establishment itself may have inadvertently added to the appeal of questionable nutritional remedies. Physicians and public health experts today urge the public to take more responsibility for changing their eating habits in more healthful directions. However, they may not ask their patients if they have questions about nutrition or provide specific advice about it in medical visits. Some patients wrongly conclude that the lack of emphasis on nutrition by health care providers is due to ignorance or a misplaced preference on the physician's part for other forms of treatment. In addition, occasionally health care professionals themselves are the source of information and advice about questionable remedies.

More attention needs to be paid to the role of effective nutritional and other life interventions in health care encounters. However, dietary measures play a role in treating some chronic diseases and conditions, but not others. When dietary measures are called for, those appropriate for disease treatment are not necessarily the same as those for preventing the disease.

USERS OF QUESTIONABLE REMEDIES

Some of the most vulnerable members of our population from the health standpoint are likely to try and use unproven remedies. There are those who suffer from chronic medical, dental, or psychological problems. In addition, the families of the handicapped and those with special health care needs are especially vulnerable to their allure.

Specific age groups may be particularly vulnerable to questionable nutritional remedies. Over 60% of all health fraud victims are older adults. Older people are particularly susceptible to false claims, perhaps because they think that questionable remedies offer simple, inexpensive ways to prevent aging, guarantee health, and relieve pain. In addition, older people suffer from chronic degenerative diseases and conditions that wax and wane in their course and for which there are no definitive cures.¹¹ Depending on the therapy in question, individuals of all ages may engage in the use of questionable therapies.

Within these broad groups, individuals with certain characteristics seem to be particularly vulnerable to questionable dietary remedies. They are often well educated, sophisticated, and intelligent individuals, who want to take an active role in their own therapy. Users of questionable therapies often have less trust in conventional medicine,¹² or have had negative experiences in dealing with health professionals. Other situational factors, such as characteristics of the disease, the attitudes of the therapist, and sociocultural factors may also be involved. Many patients use conventional and questionable therapies simulta-

neously, but do not inform their physicians that they are doing so, because they fear disapproval.

SOME POPULAR QUESTIONABLE REMEDIES

The use of questionable therapies is very widespread, and pervades both medical, dental and psychological maladies, as the following examples illustrate.

Chronic Medical Conditions: Cancer. Some of the most popular questionable cancer therapies used at present include diet. Iscador, an extract of mistletoe, is used in combination with vegetarian diets and other measures for cancer as well as for the acquired immunodeficiency syndrome (AIDS). Other vegetarian regimens are also currently popular. They include the Gerson regime, (a low salt, high potassium, vegetarian diet with various pharmacological agents, and coffee enemas), macrobiotic diets (consisting largely of cooked vegetables and whole grains as part of an overall macrobiotic philosophy and belief system incorporating many aspects of daily living) the Block Therapy (which employs conventional cancer treatment coupled with stress reduction, exercise, psychological support, and modified macrobiotic diet without the ideological underpinnings of macrobiotics), and the Livingstone Wheeler regimen (a vaccine, with antibiotics, vitamins, mineral supplements, and a special vegetarian diet that is low in fat and high in fiber, with psychological and behavioral components often used in conjunction with conventional cancer therapy). The Livingstone-Wheeler regimen was found to provide no improvement in quality of life or in survival over conventional treatments in one recent study.⁶ Other dietary regimens include the Revici therapy, which involves lipids and lipid-based substances, and the Kelly therapy, a complex nutritional program including dietary guidelines, vitamin and enzyme supplements, and "metabolic typing." Orthomolecular psychiatry is a form of psychotherapy, the benefits of which are largely undemonstrated, that use massive doses of a variety of vitamins, minerals, and food constituents (eg, laetrile or vitamin B₁₇ procaine hydrochloride, Gerovital H3 or pangamic acid [vitamin B₁₅], other substances, such as flavinoids, and other vitamin mineral supplements. Supplements of various sorts are also popular. Antineoplastins are peptides or amino acids derived from urine and popularized by Burzynski's followers.

Eumetabolic therapies consist of drugs, vitamins, minerals, plant extracts, elimination diets and therapeutic diets of various sorts which are purported to cure the cancer.

"Middle Ground" therapies have also become increasingly popular in recent years. They involve questionable psychological, behavioral, and dietary therapies applied along with mainstream standard conventional cancer treatments. They are particularly pernicious since they lend an aura of respectability to pseudoscientific measures. A detailed critique for each therapy, and many other questionable cancer therapies, is given in a recent American Cancer Society (ACS) publication on these and other questionable cancer therapies.¹³ The journals and publications of the ACS, State Cancer Society offices, and the 1-800 CANCER hotline are also good sources of information.

Other Chronic Diseases. Patients who suffer from other chronic diseases and conditions that are severe, have an uncertain course, involve considerable morbidity (such as obesity or arthritis) or mortality (such as AIDS) and lack totally effective treatments also turn to unproved dietary therapies. These are discussed elsewhere.^{14,15}

Chronic Dental Problems: Temporomandibular Joint Dysfunction. Temporomandibular joint dysfunction (TMJD) describes many different disorders causing pain and discomforts in the temporomandibular region, where the jawbone joins the temporal bone. TMJD causes pain and muscle spasm in the temple and the cheek, limited jaw motion, and clicking or popping of the joint. Among the most common demonstrated causes of TMJD are external trauma to the joints or muscles of the jaw or their malfunction, occlusal problems such as poor bite or misaligned jaw, and habits, such as clenching, excessive gum chewing, and bruxing. Degenerative joint disease, inflammatory joint disorders, and growth disorders may also cause TMJD.

The most helpful treatments for TMJD are conservative, reversible therapies, which bring symptomatic relief to many patients.¹⁶ They include analgesics, muscle relaxants, anti-inflammatory agents, moist heat, physical therapy, psychological counseling, biofeedback, temporary prosthetic devices, and electromyography, depending on the individual case. When these fail, other treatments are intramuscular and intra-articular injections into the temporomandibular joint region or surgery.

Some dentists and patients believe that dietary deficiencies are involved in TMJD. Among the questionable nutritional approaches used to treat TMJD syndrome are applied kinesiology to relax muscles. Dietary treatment involves either a diet that eliminates all refined sugar, or the addition of supplements consisting of large doses of vitamins A, C, E, B complex, calcium, and magnesium. Other dietary therapies involve supplements of vitamins A, C, B₁₂, iron, zinc, and protein. Finally the use of L-tryptophan to reduce pain has been suggested. There is no evidence from placebo-controlled trials that attests to the effectiveness of any of these measures. Elimination of gum chewing and a "soft" diet to rest the jaw may help to control pain, but they too have never been shown to be effective.¹⁷

Women's Health Problems. Increased interest in women's health issues has been accompanied by a proliferation of questionable nutritional remedies for various gynecological problems and complaints.

Premenstrual Syndrome. Premenstrual syndrome (PMS) involves chronic late luteal phase dysphoria sufficiently severe to cause marked impairment in social or occupational functioning.¹⁸ The subjective reports of psychological and somatic symptoms occur consistently after ovulation but prior to the beginning of menstrual flow, and cease for at least a week after menses. The most common symptoms are breast swelling or pain, pelvic pain, headache, skin disorders, backache, weight gain, mood swings, irritability, depression and anxiety.

Many questionable nutritional therapies are employed to treat PMS although evidence of their efficacy is lacking. These include anti-hypoglycemic diets, supplements of ω -6 fatty acids with evening primrose oil or other oils rich in these fatty acids, magnesium supplements, vitamin E supplements, abstinence from caffeine, and treatment with large amounts of vitamin B₆. In our recent review of these various theories, we found no acceptable evidence that poor diet or dietary deficiencies cause PMS or that dietary therapies cure it.¹⁹ Randomized, double-blinded, placebo-controlled clinical trials are lacking for the determining if avoidance of caffeine-containing foods, restriction of sodium or of fluids alleviates symptoms. We need for more research on the complicated hormonal and psychological

relationships that may be involved in causing the syndrome; however, at present, nutritional remedies do not offer promise.

Sex Selection by Dietary Means. Some prospective parents long to control the sex of their offspring. A questionable nutritional therapy involving an elaborate series of dietary prescriptions for the prospective mother is currently popular.²⁰ The theoretical rationale for such recommendations is implausible, and there is no acceptable evidence that such dietary measures are efficacious.²¹

Vaginal Yeast Infections. Among the questionable nutritional remedies for vaginal yeast infections and for the candidiasis hypersensitivity syndrome are a sugar-free, yeast-free diet coupled with antifungal medications popularized by William G. Crook's book.²² The American Academy of Allergy and Immunology found no basis for the dietary measures suggested.²³ More recent information also fails to confirm the utility of such dietary measures.^{24,25}

CHILDREN WITH SPECIAL DEVELOPMENTAL AND HEALTH NEEDS

Fasting therapies and elimination diets (which eliminate whole groups of foods for questionable therapeutic purposes), pose risks of growth failure and nutritional deficiencies, especially when they are used in growing children for juvenile arthritis or emotional disturbances.

Megadoses of vitamins and minerals are often used by the parents of children with mental retardation, Down syndrome, and hyperkinesis, to cure these conditions.^{26,27} There is no evidence that doses of vitamins and minerals in amounts in excess of the Recommended Dietary Allowances are helpful in these conditions. Large doses of specific vitamins are helpful in vitamin dependency syndromes, which involve specific metabolic defects. However, these states are very rare, and sound pediatric practice evidence from biochemical tests is necessary before prescribing such treatment.²⁸

WHAT CAN HEALTH PROFESSIONALS DO?

Health professionals and responsible individuals in government can take several steps to lessen the burden on patients imposed by questionable nutritional remedies. First, health professionals need to continue to improve their active listening skills and to develop more empathetic ways of relating to their patients. It is important that we all remember to treat the whole patient, not only the disease.

Second, they can improve reporting systems on the adverse effects of questionable unconventional treatments. This might be under the aegis of the State Department of Health or some other authoritative body.

Third, professional and voluntary associations should inform and educate the patients they deal with about nutritional issues involving chronic medical, dental, and emotional diseases. The American Dietetic Association currently operates a toll-free hot-line for general nutrition related questions. It is 1-800-366-1655. Its address is American Dietetic Association, 216 West Jackson Blvd, Chicago Illinois 60606-6995. The Food and Drug Administration's Regional Offices, State Departments of Health, and the Cooperative Extension Service are helpful information sources.

Fourth, more publicity needs to be given to the actual outcomes and costs of questionable nutritional remedies. Negative results tend to be ignored by the press, so consumers are often left with the false impression that the

therapies really are effective. In fact, the patient may never have had the disease to begin with, the disease continues to progress in spite of the use of the remedy, or positive effects are actually due to other more conventional therapies that are also being used.

Fifth, laymen, such as health food store operators, who often give extensive advice about disease treatment may be practicing medicine without a license. These and other individuals should also be discouraged from doing so, by legal means, if necessary.

Sixth, many questionable nutritional therapies are promoted or prescribed by health professionals. Voluntary and professional associations need to take a more active role in educating their members about questionable nutritional therapies, and the differences between them and more efficacious measures. Although many health professionals and others who use or encourage the use of questionable nutritional remedies sincerely believe that they work, and gain no particular financial or other advantage from advocating their use, ignorance is no excuse. In times such as these, when the application of many efficacious therapies is limited because of lack of resources, professional associations cannot continue to overlook or condone by inaction of their part the prescription of questionable nutritional therapies by their members. Physicians, osteopaths, nurses, pharmacists, some nutritionists, and chiropractors need to become more knowledgeable about clinical nutrition.

Seventh, licensing boards and self-regulatory activities by professional groups need to take a more proactive role in dealing with the use of questionable nutritional therapies by health professionals. In some cases, public monies are used to pay for such in efficacious treatments. Some individuals who know better (or who should know better) promote the use of nutritional remedies for disease for financial gain or other selfish reasons. A quack is a charlatan; a person (either a health professional or layman) who advertises or promotes fraudulent and inefficacious cures for disease. Fraud involves criminal deception and deceitfulness, using false representations to obtain unjust advantage or to injure the rights of others. The point at which honest error becomes fraud is a legal decision. Health professionals who persist in the use of questionable nutritional therapies for disease treatment may be engaging in malpractice. When education fails, professional societies need more explicit sanctions and systems for mandatory re-education and supervised probationary practice for health professionals who continue to advocate the use of questionable therapies after they have been apprised of the error of their ways.

Eighth, we need more efforts to ensure that questionable nutritional therapies are not being used in public hospitals are clinics. For example, in a New England State, debilitated AIDS patients who were being treated in a state chronic disease hospital for the medically indigent and their families were solicited by a professional staff worker who held a doctoral degree in biochemistry to buy a

megadose vitamin supplement regimen which cost over a \$100 a month. Legal means should be employed to remove such quacks who practice nutritional fraud on unsuspecting patients from government facilities.

Acknowledgments. Preparation of this manuscript was supported in part by Grants MCJ9120 and 8241 of the Maternal and Child Health Services, US Department of Health and Human Services, and by Grant R01CA54349 from the National Institutes of Health.

REFERENCES

1. American Cancer Society: Questionable methods of cancer management. Atlanta, GA: American Cancer Society (in press 1992).
2. Markman M: Medical complications of "alternative" cancer therapy. *N Engl J Med* 1985; 312:1640-41.
3. Herbert V: Unproven (questionable) dietary and nutritional methods in cancer prevention and treatment. *Cancer* 1985; 58:1930-1941.
4. Dalton MJT: Characteristics of pyridoxine overdose neuropathy syndrome. *Acta Neurol Scand* 1987; 76:8-11.
5. Slutsker L, Hoesly FC, Miller L, et al: Eosinophilia—myalgia syndrome associated with exposure to tryptophan from a single manufacturer. *JAMA* 1990; 264:213-217.
6. Cassileth BR, Lusk EJ, Guerry D, et al: Survival and quality of life among patients receiving unproven as compared with conventional cancer therapy. *N Engl J Med* 1991; 324:1180-1185.
7. Grigg W: Quackery: it costs more than money. *FDA Consumer* (July/August) 1988, pp30-32.
8. Cassileth B, et al: Contemporary unorthodox treatments in cancer medicine. *Ann Int Med* 1984; 101:105-112.
9. Gambrill E: Self-help books: pseudoscience in the guise of science? *Skeptical Inquirer* 1992; 16:389-399.
10. Jones LM: The two cultures: a resurrection. *Skeptical Inquirer* 1989; 14: 57-60.
11. Chapman N, Sorenson A, Ory M, et al: Nature, causes and consequences of harmful dietary practices: implications for older people. *Clin Appl Nutr* 1991; 1:32-50.
12. Louis Harris and Associates: Health information and the use of questionable treatment: a study of the American public. Washington DC, US Department of Health and Human Services 1987.
13. American Cancer Society: *Questionable Methods of Cancer Management*. Atlanta, American Cancer Society, 1992.
14. Dwyer JT: Nutritional remedies: reasonable and questionable. *Ann Behav Med* 1992; 14:120-125.
15. Dwyer JT: Treatment of obesity: conventional programs and fad diets, in Bjorntorp P, Brodeff BN (eds): *Obesity*. Philadelphia, JB Lippincott, 1992, pp 662-676.
16. Solberg WK: Temporomandibular disorders: background and the clinical problems. *Br Dent J* 1986; 160:157-61.
17. Thompson T, Dwyer JT, Palmer CA: Nutritional remedies for temporomandibular joint dysfunction: fact or fiction? *Nutrition Today*, Jan/Feb 1991, pp37-42.
18. American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders III* ed 3, revised. Washington DC, American Psychiatric Association, 1987.
19. Casey V, Dwyer JT: Premenstrual syndrome: theories and evidence. *Nutrition Today* 1987; pp4-12.
20. Langedoen S, Proctor W: *The Preconception Gender Diet*. New York, M. Evans and Co, 1982.
21. Palmer CA, Dwyer JT: Boys or girls by the flick of the fork? The questionable basis of the preconception gender diet. *Nutrition Today*, March/April 1992, pp32-36.
22. Crook WG: *The Yeast Connection: A Medical Breakthrough* ed 3. Jackson, Tennessee, Professional Books, 1989.
23. American Academy of Allergy and Immunology: Candidiasis hypersensitivity syndrome. *J Allergy Clin Immunol* 1986; 78:271-273.
24. Bennett JE: Searching for the yeast connection. *N Engl J Med* 1990; 323: 1766-1767.
25. Barrett S: Candidiasis hypersensitivity. *Nutrition Forum* 1987; 4:84-85.
26. Omaye ST: Safety of megavitamin therapy. *Adv Exp Med Biol* 1984; 177:169-203.
27. Haslam RHA, Dalby JT, Rademaker AW: Effects of megavitamin therapy on children with attention deficit disorders. *Pediatrics* 1984; 74:103-111.
28. Barnes LA: Adverse effects of overdosage of vitamins and minerals. *Pediatrics in Review* 1986; 8:20-25.

Health foods and supplements for the elderly

Who can say no?

DAPHNE A. ROE, MD

Elderly men and women are frequent users of unproven and fraudulent nutrition products because they want to believe the claims made, that these may retard aging and bring symptom relief. They are especially targeted as purchasers of tonics, questionable nutrient mixtures, herbal remedies and rejuvenating cosmetics, by persuasive advertisements in magazines for the elderly as well as by TV and newspaper advertising. Such products are available in health food stores, pharmacies, supermarkets, and from mail order houses. Risks from using these products include both the hazards of vitamin and drug toxicity as well as the delay in seeking medical care. The public need education about these risks, and product regulation is urgently required.

To understand why the elderly are misled into believing that health foods and nostrums are useful as a means to achieve better health and to overcome the symptoms of chronic disease, it is important to understand the persuasiveness of the health claims and the vulnerability of those who are deceived.

Health and nutrition claims by individual nutrition quacks and by organizations that make the sale of health foods their business are persuasive because, as pointed out by Victor Herbert,¹ they oversimplify and exaggerate the potential of nutrients to prevent chronic disease. They also may make claims for foods and nutrients which are totally false. Furthermore, they may adopt a mystique which suggests that food substances that have the respectability of an ancient folklore to support their health-promoting properties (eg, garlic), can alter health destiny.

REASONS THE ELDERLY ARE TARGETED FOR HEALTH FOODS AND FRAUDULENT NUTRITION PRODUCTS

The elderly are targeted for health foods and related products both because the purveyor of such products may believe in their efficacy to offset the effects of aging, and because the less scrupulous vendor, even if unbelieving, hopes to persuade the elderly to use their brand of nutrition magic.

The worthless nutrition and food products intended for sale to the elderly are likely to bear claims indicating use in combatting symptoms of common chronic diseases which are prevalent in older people. In his book on the history of health quackery in 20th century America, James Young² has collected reasons proposed to explain the susceptibility of particular subgroups of the population to health and nutrition fraud. Those with chronic disease are identified as being most vulnerable. They may not be intellectually taken in by the advertising gimmicks of the vendors of health and nutrition quackery, but they may allow themselves to try out what is offered on the slim chance that it will work. One

group of chronic disease sufferers who are generally recognized as being susceptible to fraud are those with chronic arthritis whose symptoms are unrelieved by the medical treatments they have received. Their susceptibility to health fraud is engendered not only by unrelieved symptoms, and particularly pain, but also by feelings of discouragement. It is suggested that those with chronic painful diseases are more willing to try quack remedies since they feel they have nothing to lose. Intelligence and knowledge that the quack remedy is unlikely from the scientific standpoint to offer hope of cure, may not be a defense against a trial of a phony treatment. The arguments of the vendor of quack remedies may be persuasive both to those who are unsophisticated in their selection of treatment modalities and to those who are sophisticated, but are discouraged by past experience of the outcome of accepted medical treatments.

Because the elderly form the subgroup of the population with the highest prevalence of chronic disease and disability which is not amenable to lasting relief by approved drug, diet, surgical, or physical therapy, they may seek alternate means of relief from their medical problems. However, experience indicates that acceptance of quack remedies and quack nutrition treatments by the elderly is also linked to their being deliberately targeted by the purveyors of worthless products. Not only may the elderly wish to seek relief from the pain and stiffness of degenerative arthritis, but many also seek to improve their failing memory and lessen other common symptoms of geriatric health problems.³

The need to seek positive health, and to prevent loss of health with aging, may explain the use of high-potency vitamins and tonics which advertise such efficacy.⁴ Perceived reduction in health care costs achieved by buying nutrition products rather than incurring medical bills for office visits, may also influence decision making.

HEALTH FOODS AND NUTRITION PRODUCTS PRESENTLY AVAILABLE

Tonics and Nutrient Mixtures. In the past, tonics were mixtures of bitters in an alcohol-containing vehicle that were used to stimulate appetite. Often iron salts were added to treat anemia, which was considered to be a cause of loss of appetite. Today the lay public consider tonics and nutrient mixtures to possess many of the same properties. False advertising fosters the belief that tonics containing vitamins and minerals in an alcohol-containing base will give you pep and energy. These products commonly have a "Geri" prefix.⁵ Nutrient mixtures as well as extracts of plants which are questionable sources of nutrients, are also considered to be "strengthening." These products are thought to be most valuable if they come from natural sources. In addition, traditional use of the products in folk medicine increases their perceived value for health promotion. Thus, products containing aged garlic and Siberian ginseng extract may be attractive to the gullible.

From the Division of Nutritional Sciences, Cornell University, Ithaca, NY 14853.

Address correspondence to Dr Roe, Professor of Nutrition, Division of Nutritional Sciences, Cornell University, Savage Hall, Ithaca, NY 14853.

Products available in health food stores for use by the elderly include those said to contain a very large number of ingredients of plant origin which are claimed to increase energy. One such product is advertised to contain "a multivitamin with whole food concentrates." It is further stated to provide "the natural energy of over 65 wholesome food factors, including spirulina, chlorella, wheat grass juice and sprouted barley juice." In addition, this mixture is said to contain "advanced" mineral forms like chelates and citrates, antioxidants and other nutritional advances of the last billion years.

A popular magazine which, because of its name, is clearly intended for reading by older men and women, carries advertisements such as the following: "Fatigued? Revitalize with ancient Chinese ginseng/royal jelly liquid formula. 10 day supply \$9.95. Herb, vitamin catalogue \$2.00" and "A 57 nutrient herbal formula which 'seems to purify and oxygenate the blood.' \$37.00 for a one month supply."

Certain of the nutrient mixtures sold are said to contain male formula and female formula. It is implied that the addition of these products increases sexual performance.

Rejuvenating Cosmetics. There are several types of rejuvenating cosmetics, including those that claim to tighten wrinkled skin, to lighten age spots, and to generally rejuvenate the skin. The rejuvenating cosmetics often contain vitamin E for topical use.

Other ingredients of such products, intended to bring back a youthful skin, are substances which might infer a food origin such as "fresh plant butters." The mistaken idea that the skin can be fed by topical applications, is encouraged. Facial creams containing vitamin E are definitely preferred and it has been recently claimed that one such cream returns the skin to a healthy and radiant state in just seven days.

A risk of actinic damage and skin cancer may be associated with the use of products that claim to "tan and protect." One such product is stated to be PABA- and benzophenone-free and contains vitamins A, C, D, and E. This information may well mislead those elderly, at risk for skin cancer, who are ignorant of the fact that presently PABA and benzophenone are two of the most important topical sunscreens and that topical preparation of vitamins A, C, D, and E have no such protective effect.

Hair Growth Stimulants. Certain vitamin-mineral mixtures are sold to stimulate hair growth or regrowth in balding men and in older women whose scalp hair is getting thin. One such product is advertised as a "nutritional thick-shake for healthy hair." According to this advertisement, 60% of Americans lack adequate amounts of vitamin A. The product is defined as "hair tablets," and is said to contain a combination of vitamin A and L-cysteine to improve hair texture, vitamin B₅ and inositol or folic acid for thinning hair, vitamin A and C, as well as unsaturated fatty acids to correct deficiencies, and folic acid, pantothenic acid and B complex for restoration of hair color. Two tablets are recommended per day. However, in the advertisement no actual information is given about the concentrations of these nutrients present. A patient of the author took six tablets a day of a similar product to encourage hair and nail growth and developed vitamin A toxicity with patchy alopecia and abnormal liver function tests.⁴

Weight Control Products. These products claim to include nutrients that are essential to older men and women who are on low calorie diets, and the products are available "at bargain prices." When advertised in maga-

zines, a check or money order is requested with the come-on of the term "satisfaction guaranteed." One such product was stated to be a source of chromium picolinate, to "trigger fat loss and lean muscle enhancement." However, there is no evidence to support these claims!⁵

Waters to Promote Energy. An example is the "energetic water" produced by a firm in Traverse City, Michigan. This water is claimed to be "Many times purer than distilled, filtered or reverse osmosis [waters]."⁶

Natural Products to Relieve Depression and Induce Sleep. Tryptophan supplements have been sold as a treatment for depression and as a natural product to promote restful sleep, both for the elderly and for younger adults. Tryptophan has been sold as an antidepressant, although its effectiveness for this purpose has been questioned.⁶ Doses of 1-5 g have been recommended for the purpose of sleep induction. The sale of 0.5 g tablets of tryptophan as a sleeping pill was common until recently when tryptophan supplements were found to be the cause of the eosinophilia-myalgia syndrome.⁷

Anti-Aging Products. Certain products claim to prevent aging itself, including a herbal mixture containing thyme. Apparently no pun on the word "time" is implied!⁸

Cancer-Prevention Products. In a magazine recently found on the check-out counter at a grocery market, garlic was stated to "ban skin cancer." Since the size of the print was extremely large, it is likely that few elderly clients would have missed it. Other serious sources of misinformation are claims such as the one seen by the author on a large placard in a pharmacy in New York City, which stated "Take beta carotene. It reverses the effects of smoking."

SOURCES OF ADVERTISING

The nutritional products under discussion are advertised in magazines, in local newspapers, and in health food stores. In addition, they may be extolled in books that describe methods to retard aging by dietary means. Anti-aging cosmetics sold in pharmacies may also be labelled to indicate their beneficial effects. TV and radio advertisements may be used and the products may be extolled on placards.

SOURCES OF SUPPLY

These nutritional products can be obtained through mail-order houses that accept credit cards or checks. In addition, they are sold in health food stores, pharmacies, supermarkets, and from individual offices of chiropractors.

PERCEIVED BENEFITS

Cost v Rx Drugs. The elderly will often buy nutrient or other food supplements of the worthless type, because of apparent savings in cost over use of prescription drugs. Benefits relative to cost may be short-lived because of a subsequent need to purchase prescription drugs. Furthermore, as indicated by the advertisements quoted here, the cost of nostrum may be high, particularly if they are used frequently in large amounts, and/or if multiple supplements are used.

Possible Positive Effects on the Immune System. Single nutrients including vitamin E, zinc, and beta-carotene may promote immune function in the elderly.⁷⁻⁹ However, modulation of the immune system by these nutrients is more appropriately carried out under medical supervision and using single nutrients prepared under quality control

rather than with vitamin or vitamin-trace element mixtures of unknown purity.³

Sleep-Promoting Effects. A recent text on symptom control states that "there is some evidence that L-tryptophan induces sleep when taken in doses of one gram at night."¹⁰

REAL RISKS

Vitamin Toxicity. The elderly incur special risks from vitamin toxicity. For example, it has been shown that increases in plasma levels of vitamin A are greater in the elderly than in younger individuals after dosing. This may be explained by increased absorption of the vitamin with aging that has been reported.^{11,12} Other factors contributing to the risk of vitamin A toxicity in the elderly include the presence of liver and kidney disease. Alcoholic liver disease in the elderly imposes a special risk for vitamin A toxicity. It has also been mentioned that those elderly who may be in the habit of taking vitamin E supplements may increase the risk of vitamin A toxicity because vitamin E may promote vitamin A absorption.²

Risk of Supplement Contaminants. In the last two years, L-tryptophan-containing products have been found to be the cause of the eosinophilia-myalgia syndrome. This is a multisystem disorder affecting muscles, skin, and fascia, as well as being associated with a vasculitis which is due to a contaminant that was developed in the course of the Japanese manufacture of tryptophan supplements. The numbers of people affected with this condition have been argued with estimates as high as 10,000. However, from early 1990 until May 1992, 1,511 cases and 38 deaths have actually been reported to the Centers for Disease Control. The oldest person reported to have the eosinophilia-myalgia syndrome was 85-years old.¹³ The recent epidemic of eosinophilic-myalgia, possibly due to a contaminant in tryptophan supplements, has assuredly brought home the danger of products being sold which are not under quality control.³

Drug Toxicity. The elderly are more at risk from misuse and overuse of vitamins than younger adults because of the therapeutic drugs they take. For example, elderly who take β -adrenergic-blocking drugs as antihypertensive agents and who concurrently take pharmacologic doses of niacin on the supposition that the niacin may improve memory by dilating cerebral vessels, may develop syncope.⁴

Delay in Seeing an MD. Reliance on worthless nutritional products to treat symptoms may delay treatment of serious health problems. In this regard, however, it is important to mention that the elderly may buy mail order nutritional products because of difficulties in getting to the doctor, because of lack of transportation, or because they cannot afford office visits.⁵

Not Taking Appropriate Rx Drugs. Elderly may take nutritional products as a substitute for appropriate therapeutic drugs, particularly if the drugs they have been prescribed induce unpleasant side effects or are not effective in bringing about symptom relief.

PREVIOUS ATTEMPTS AT STATE ACTION TO COMBAT HEALTH AND NUTRITION FRAUD AGAINST THE ELDERLY

The Republican Task Force on Health Fraud and the Elderly of New York State proposed legislation in 1986 that would strengthen false advertising statutes relative to health products, that would give the media assistance in self-regulation, create a Health Fraud Task Force within

the State Attorney General's Office, expand FDA jurisdiction with regard to health fraud, and that would educate the public about developments in the area of health fraud.¹⁴ Barriers to the implementation and enforcement of more stringent regulations in the sale of health and nutrition products to the elderly were discussed at public hearings at that time. The chief points that were made are as follows:

1. Often the products purchased do not carry false claims but rather the advertisement for the product misinforms the prospective customer.
2. The elderly often rely on mail order purchase of products which might escape regulation.

At the time of the hearings on the proposed legislation, several important recommendations were made by representatives of professional societies. For example, a representative from the New York State Dietetic Association emphasized the need for licensing those who practice nutrition counselling, and also emphasized that the elderly need to be better educated about the risks of health and nutrition fraud.

GUIDELINES FOR ACTION BY HEALTH CARE PROVIDERS NOW

Education of Elderly Patients. Health care providers including physicians, nurses, dietitians, and pharmacists need to educate the elderly about the risks of worthless nutrient supplements and related products that impose health risks. The benefits of obtaining medical advice on health problems need to be stressed. However, unless the elderly have better means than now exist for accessing the medical care system, it is likely that they will still be tempted to buy the products of present concern. Furthermore, it is unlikely that educating the elderly will prevent the purchase of nostrums as long as symptom relief is still a hard-to-come-by commodity for many disabled elderly.

Resource Information Available on Worthless and Dangerous Nutritional Products. Health care providers and agencies providing services for the elderly should have information available about worthless and dangerous nutritional products that should be avoided.

New Legislation. A new effort should be made to promote the regulation of health foods and related products at the state and federal level.

REFERENCES

1. Herbert V: The health hustlers, in *The Health Robbers*. Philadelphia, George F. Stickley Co, 1976, pp100-123.
2. Young JH: *The Medical Messiahs: A Social History of Health Quackery in Twentieth Century America*. Princeton, NJ, Princeton University Press, 1967, pp423-433.
3. Blumberg JB, Suter PM: Pharmacology, nutrition and the elderly: Interactions and implications, in Gaithersburg MD (ed): *Geriatric Nutrition: The Health Professionals' Handbook*. Aspen Publishing Inc, 1991, pp337-361.
4. Roe DA: *Diet and Drug Interactions*. New York, Van Nostrand Reinhold, 1989, pp105-134.
5. Roe DA: *Alcohol and the Diet*. Westport, CT, AVI Publishing Co, 1979, pp208-222.
6. Linder MC: Nutrition and metabolism of proteins, in Linder MC (ed): *Nutritional Biochemistry and Metabolism with Clinical Applications* ed 2. New York, Elsevier, 1991, pp87-109.
7. Meydani SN, Barklund MP, Liu S, et al: Vitamin E supplementation enhances cell-mediated immunity in healthy elderly subjects. *Am J Clin Nutr* 1990; 52:557-563.
8. Duchateau J, DeLeprasse G, Urigens R, et al: Beneficial effects of oral zinc supplementation on the immune response of old people. *Am J Med* 1981; 70:1001-1003.
9. Watson RR, Prabhala RH, Plezia PM, et al: Effect of carotene on lymphocyte subpopulations in elderly humans: evidence for a dose response relationship. *Am J Clin Nutr* 1991; 53:90-94.
10. Walsh D: *Insomnia*, in Walsh TD (ed): *Symptom Control*. Oxford, England, Blackwell Science Publishing, 1989, p278.
11. Russell RM: Malabsorption and aging, in Bianchi L, Holt P, James

OFW, et al (eds): *Aging in the Liver and Gastrointestinal Tract*. Lancaster, England, MTP Press Ltd, 1988.

12. Suter PM: Vitamin requirements, in Gaithersburg MD: *Geriatric Nutrition: The Health Professionals' Handbook*. Gaithersburg, MD, Aspen Publishing Inc, 1991, pp25-52.

13. Roufs JB: Review of L-tryptophan and the eosinophilia myalgia syndrome. *J Am Diet Assoc* 1992; 92:844-850.

14. Health Fraud and the Elderly. A special report prepared by the Assembly Republican Task Force on Health Fraud and the Elderly. New York State Assembly, 1987.

Sports nutrition fraud

SARAH H. SHORT, PhD, EdD, RD, LEONARD F. MARQUART, PhD, RD

As far back as Ancient Greece, Olympic athletes were in pursuit of a magical food that would enhance sports performance. Today, more than ever, athletes are searching for the "competitive edge," since the difference between winning the gold and placing out of medal contention may be a hundredth of a second or fractions of a point (the 1992 Olympics, Barcelona, Spain). Athletes may turn to ergogenic aids (performance enhancers) to provide an advantage.

General categories of ergogenic aids and examples are described by Williams¹ and include biomechanic (lighter running shoes), psychologic (hypnosis), pharmacologic (anabolic steroids), physiologic (blood doping), and nutrition aids (protein powders). The focus of this paper is on controversial dietary substances marketed to athletes.

There are several problems connected with nutrition information and products for athletes, as well as for the general public. The Federal Food, Drug, and Cosmetic Act is the law that protects consumers against harmful and misleading food, drugs, devices, and cosmetics.² However, the Proxmire Amendment³ modified the law so that the Food and Drug Administration (FDA) cannot set limits on the potency of vitamin and mineral supplements except for reasons of safety, and cannot declare them drugs only because they exceed the level of potency determined to be nutritionally rational or useful. According to FDA Deputy Associate Commissioner Dykstra "... it is no secret that in terms of safety of dietary supplements, FDA is not doing much today. It is really 'buyer beware!'... The framework simply is not in place today to give consumers the type of assurance that they demanded."⁴ Recently, the FDA Dietary Supplement Task Force has been investigating vitamins and minerals, amino acids, and a "catch-all" category (including such products as coenzyme Q-10, garlic oil, and herbs) for safety and nutritive value among other concerns. It is hoped that athletes, as well as the general public, soon will be better protected when they buy dietary supplements.

Another problem is that nutrition books published for the public can be inaccurate or false because of First Amendment rights of free speech. Furthermore, anyone may be called a nutritionist. A nutritionist may be someone who purchases a degree from a non-accredited institution, a PhD in nutrition, a physician who specializes in nutrition, a dietitian, or others. A registered dietitian RD is someone who has graduated from an accredited university, an internship or similar experience, passed an examination

given by the American Dietetic Association, and has continuing education credits.⁵ Dietitians can also be licensed by some states and use LD after their names. Athletes should ask for credentials before they follow nutritional advice.

An added problem is that research scientists sometimes go public with their conclusions before their study or experiments have been duplicated or subjected to peer review. One research study or one epidemiological survey does not test a scientific theory. Since athletics are big business in the United States, all of these problems are intensified when it comes to sports nutrition information and products. Misinformation spreads through electronic and print media to the players, their coaches, and trainers. "There is a growing need for sports nutrition counseling and education to help athletes improve their eating habits."⁶

In many cases, advice (including supplementation) for athletes is presented as if all athletes had the same needs. Nutrition advice must be individualized. When providing nutritional information, it is necessary to know if the athlete is involved in an endurance or short-term event, body composition (if possible), age, time spent practicing and training, and whether the athlete is training for a meet/match/tournament lasting one day or held on successive days. Nutrition advice that is provided for "athletes in general" makes little sense.⁷

Since proper training, coaching, and diet cannot guarantee success, athletes often resort to nutritional supplements. A recent survey of nutritional supplements in health and bodybuilding magazines found "89 brands, 311 products, and 235 unique ingredients, the most frequent of which were unspecified amino acids..."⁸ In 1990, the Council for Responsible Nutrition estimated that retail sales of nutritional supplements was \$3.3 billions.⁹ Unfortunately, most of these product manufacturers have not presented research that demonstrates their claims. Lightsey, the coordinator for the National Council against Health Frauds Task Force on Ergogenic Aids has outlined a number of deceptive tactics used in selling these products.¹⁰ These include published research taken out of context, claims of "university tested" when no research was done, unauthorized endorsement by professional organizations, false statements that research is currently being performed, testimonials, inappropriately referenced research, patented products (not of proof effectiveness), mass media publicity, and others. Even the most informed athletes may not be able to calculate the risk-to-benefit ratio of the newest product hitting the market, nor care about long-term effects.

From Syracuse University, Syracuse, NY (Dr Short) and Cornell Cooperative Extension, Mexico, NY (Dr Marquart).

Address correspondence to Dr Marquart, Cornell Cooperative Extension, Oswego County, Mexico, NY 13114.

The younger athletes may be the most frequent users of these supplements, and they may encounter larger risks. A review of 30 (now 50) studies involving athletes and vitamin/mineral supplementation found a range in use between 6% and 100% with "most studies reporting that more than half of the athletes consumed supplements."¹¹ There is a definite need for more data (using larger sample sizes) to investigate the prevalence, frequency, duration, and type of nutritional supplements used by various athletes' populations.

Several factors may contribute to the athletes' increased use of nutritional supplements. Adequate sports nutrition or even general nutrition knowledge is lacking.^{6,12} Most athletes surveyed could not pass a test of basic nutrition knowledge, although they did slightly better on sports nutrition questions. Certified athletic trainers earned higher scores on nutrition tests than athletes or coaches. Coaches indicated that they (as coaches) should provide nutrition information to the athletes, although few had any formal nutrition training. Many coaches suggested that the athletes take supplements of vitamins or amino acids. In a large study, it was found that athletes in high school and college settings ranked parents or popular media as their first or second source of nutrition education.¹³ A poor understanding of nutrition combined with slick advertisement campaigns appearing in the popular press often perpetuates myths and misconceptions regarding diet and nutritional supplements. To add to the problems, athletes appear to have a poor understanding of strategies for enhancing muscle development.

Several popular body building magazines exist to promote their nutritional products. The New York City Department of Consumer Affairs indicated that 56% of full-page advertisements for nutritional supplements in four popular body-building magazines were worthless and possibly harmful.¹⁴ The amount of money spent on these supplements can be substantial. College athletes may spend as much as \$400 per month on supplements. This is money that would be better spent on food.

There have been relatively few attempts to regulate the nutrition supplement industry at the federal, state, and local levels. This may be changing since the New York City Department of Consumer Affairs is issuing "Notices of Violation" of the New York City Consumer Protection Law for deceptive advertising against companies making product claims such as the following:¹⁴

- "A New! Advanced Cell Growth Formula That Stimulates Muscle Growth Even While You Sleep!!!"
- "watch . . . muscles explode with incredible strength, massive size, and pure energy."
- "the most powerful muscle-building amino acid."
- "pack on the muscle" and produce "huge gains in record time."

The FDA's Dietary Supplement Task Force is a step forward. They are also examining claims made by nutritional supplement manufacturers which would make the products come under the definition of a drug. Any supplement claiming to be anabolic, stimulate hormone secretion, and/or effect body structure or function are subject to drug regulations. The National Council against Health Fraud's Task Force on Ergogenic Aids has reviewed performance enhancing claims made by 45 different products.¹⁰

VITAMIN MINERAL SUPPLEMENTS

The Committee on Diet and Health (Food and Nutrition Board, National Research Council) recommends that the

American public avoid taking dietary supplements in excess of the Recommended Dietary Allowance (RDA) in any one day.¹⁵ It was concluded that healthy people can, and should, obtain essential nutrients from a variety of foods. Exceptions were noted in cases of pregnancy, lactation, newborns, people with malabsorption problems, women with excess monthly bleeding, people with very low caloric intake, and some vegetarians. Most athletes would not fall in any of the above categories except possibly the last three. Harper¹⁶ stated that vitamin deficiency diseases "now occur so rarely in this country as to be medical curiosities. Nevertheless, large numbers of apparently healthy people take vitamin supplements." Harper asserted that there is no proof Americans need vitamin supplements, but they do need accurate nutrition information instead of the misinformation which is so widespread. The United States National Health Interview Survey¹⁷ indicated that more than 30% of adults take vitamin and/or mineral supplements. Some adults were taking supplements 6–43× the RDA, leading to the suggestion that "excessive vitamin and mineral intakes may pose a greater hazard than nutrient deficiency for the population of the US."¹⁸ Evaluating nutrition research is difficult. Quality nutrition research studies should have at least 50 human subjects, appropriate control groups, controlled nutrient intake, adequate consumption data for pre- and post-experimental periods, a level of food consumption that is reasonable, and significant statistical results.¹⁹ Few survey studies meet these specifications.

Williams, in his excellent sports nutrition book, indicates that "all the current reputable research refutes an ergogenic effect of multivitamin-mineral supplements in adequately nourished athletes."²⁰ Others agree that vitamin supplements do not improve physical performance in those with an adequate diet.^{21,22} Clarkson extensively reviewed the effect of vitamins, minerals, and trace minerals on athletic performance.^{23,24} She found a lack of evidence that these products influence athletic performance, but athletes buy them because of advertisements in popular magazines and a lack of correct nutrition information.

Using a 9-month, double-blind, placebo-controlled study on male runners, Weight et al²⁵ found multivitamin and mineral supplementation without measurable "ergogenic effect" and concluded that this procedure is not necessary for athletes on a normal diet. The effects of a commercial dietary supplement (vitamin, mineral, plus other substances) was tested in a double-blind experiment with 20 runners.²⁶ It was concluded that the supplements had no useful effect on physiological performance. A group of French researchers concluded that "vitamin supplements should be used only on the advice of the team physician and should be strictly reserved for athletes with demonstrated biochemical deficiencies."²⁷ Since these athletes are taking "stack packs" (plastic-encased packages of a number of ergogenic products), it should be noted that the biological consequence of taking these products together has not been researched.

Single vitamins are often selected, but not without consequences. Since muscle contains up to 80% of the vitamin B₆ in the body, athletes are prone to take these tablets. A well done study showed that vitamin B₆ in skeletal muscle was not easily depleted and that supplementation with this vitamin does not significantly increase vitamin B₆ in college age men's muscle.²⁸ On the other hand, it has been demonstrated that overdoses of this vitamin can be harmful. Subjects self-dosing with from 2 g

to 6 g over a period of from 2 months to 40 months developed severe sensory nervous system dysfunction which was not totally reversible when the vitamin B₆ supplementation was stopped.²⁹

PROTEIN AND AMINO ACIDS

Advertisers claim that amino acids are a safe, effective means of enhancing muscular strength and more effective than anabolic steroids without the devastating side effects. Others claim that single amino acids are more readily digested, absorbed, and less taxing on the body than protein consumed from food.¹ In addition, protein powders and amino acid supplements have been marketed to endurance athletes under the assumption that these athletes need additional protein to replace energy stores, synthesize new enzymes and protein as a result of training.³⁰

Several studies have surveyed the use of protein supplements by athletes. Among college athletes, 98% believed performance was improved by a high-protein diet while 80% reported that large amounts of protein are necessary to increase muscle mass.³¹ Krowchuk et al³² indicated that 56% of high school athletes would consider using protein supplements. Males were more aware of nutritional supplements than females. Parr³³ reported that 9% of high school and college athletes consumed protein supplements. Males (12%) were more likely than females (10%) to take additional protein. Football and basketball players were the largest consumers of protein supplements. Of athletes who used protein supplements, 50% used 1–10 g/day, while some used up to 50 g/day. In another study involving 943 randomly selected high school athletes, 8% regularly consumed protein and dietary supplements.³⁴ Barret states that “more than 100 companies are marketing vitamin and amino acid concoctions said to increase stamina, endurance, and muscle bulk. All of these products are fakes.”³⁵ Do athletes need to take supplements or can they obtain enough from dietary intake?

While protein requirements of athletes have been researched and debated for years,^{36,37} there is a body of literature indicating that protein requirements of endurance and strength athletes are higher than their more sedentary counterparts.^{38–41} Although definitive recommendations for protein intake among athletes require further study, current evidence from Lemon⁴² suggests that strength athletes should consume 1.2–1.7 g protein/kg body weight (BW) and endurance athletes 1.2–1.4 g/kg BW.

A protein intake of 0.9 g/kg was adequate to maintain nitrogen balance in experienced body builders with sufficient energy intake.³⁷ Nutrient intake data indicate that most athletes consuming adequate calories meet the recommended protein needs. Exceptions might include athletes involved in sports requiring a certain weight classification (wrestling, boxing) or certain aesthetic appeal and a high lean body mass to fat ratio (ballet, gymnastics, diving). In a four-year study of 16 different athletic teams (554 athletes) at a major university, all athletes except wrestlers and gymnasts were receiving enough protein when calculated on a per kilogram BW basis.⁴³

The practice of consuming amino acid supplements is based on the observation many years ago that intravenous administration of some amino acids resulted in increased growth hormone release.⁴⁴ Body builders typically consume arginine-lysine or arginine-ornithine supplements under the assumption that these combinations will stimulate

growth hormone release resulting in increased muscle protein synthesis and muscle strength.

Although oral administration of certain amino acids may promote growth hormone release, there is little evidence to suggest improvement in muscle hypertrophy or functional strength as a result of this practice.^{45,46} “At present, then, there are no data to support an ergogenic effect of human growth hormone on muscle size, strength, or power beyond the effect generated by a proper weight training program.”⁴⁷ The possibility of adverse health problems seems to be high. Since there are so few well controlled studies on arginine, ornithine, other amino acids and growth hormone, further research is needed to evaluate the effects of combining amino acid supplementation and weight training in promoting strength and muscle development.

Athletes should be warned of the possible complications associated with large doses of protein and amino acid supplementation. This practice could interfere with absorption of amino acids and protein in food and lead to metabolic imbalances. Some amino acids can be potentially toxic.^{48,49} Supplementation can interfere with the consumption of a wide variety of foods and thus compromise nutritional status. The effects of elevated levels of growth hormone have not been adequately studied in healthy persons. Amino acid supplements are not recommended because of a lack of evidence to document enhanced muscle strength and size, no established margin of safety for single and combined doses of amino acids, and no studies to evaluate the risks associated with long-term use.

OTHER ALTERNATIVES TO ANABOLIC STEROIDS

A variety of products are being manufactured and marketed on the basis that they contain a natural source of testosterone or that they help stimulate endogenous testosterone levels. Glandulars or ground up animal organs are derived from hearts, livers, spleens, brains, pituitary glands, adrenal tissue, and testicles. Beef testicles, commonly sold in health food stores are “thought to be an anabolic steroid by some adolescents.”⁵⁰ The amount of testosterone sequestered in the testes is very small and is destroyed during the manufacturing process or during the human digestive process. There is no evidence that other animal organs have any effect on testosterone levels including ground up hypothalamus and pituitary which are claimed to provide athletes with the precursors for testosterone production.⁵¹

Sapogenins are found in desert plants and marketed as a plant extract or by their chemical or plant name. Some plant species that have been advertised include Smilax, trillium, yucca, and sarsaparilla. Actual sapogenins include diosgenin, smilagenin, sarsapogenin, and hecogenin. Diosgenin is a precursor used to manufacture many useful steroids. Diosgenin is being sold to athletes under the false pretense that the body will synthesize testosterone from this precursor just as chemists do in the lab.⁴⁶ The potential for toxicity may exist for some of these sapogenins as evidenced by animal studies.⁵²

The use of γ -oryzanol and plant steroids (phytosterols) have been popular among athletes.^{46,53} Oryzanol is composed of ferulates of plant sterols (Campesterol, Stigmasterol, Beta-Sitosterol, Cycloartenol). Plant sterols are found in the lipid fraction of many plants and vegetables. The structural similarities of oryzanol and phytosterols to cholesterol have led to numerous claims primarily focusing on the hormonal system. General statements regarding the effects of oryzanol supplementation obtained from product bro-

chures include the following: Gamma-oryzanol raises the natural testosterone levels; Gamma-oryzanol, a natural steroid alternative develops increased lean muscle mass and definition, "Beta-sitosterol, an oryzanol component, has a chemical structure that can be readily converted into androgens, resulting in anabolic enhancement."⁴⁸ There is no evidence to indicate that γ -oryzanol or plant sterols will elicit anabolic-androgenic activity. In fact, animal studies suggest that ingested oryzanol may depress anabolic activity. Due to poor absorption characteristics of phytosterols and oryzanol (less than 5%) the medical risks appear to be minimal.

Boron, a trace mineral, seems to affect calcium and magnesium metabolism and may be part of membrane function and bone health.⁵⁴ Borates were banned as a food preservative 40 years ago, but now boron in small amounts is believed to have a beneficial effect. Boron is pervasive in our surroundings and is easily absorbed. Hunt and colleagues⁵⁵ found that good sources of boron include fruits, vegetables, tubers, legumes, and some spices. It is also a contaminant or an ingredient of some personal care products such as antihistamines, denture cleaners, antacids, laxatives, and lipsticks. An article published in 1988 stating that boron was an overlooked element of nutritional importance amazed the author, Nielsen, with its consequences.⁵⁶ Claims appeared that boron could increase muscle mass and strength in athletes although the research had shown that boron supplementation only increased testosterone in postmenopausal women. Nielsen noted that postmenopausal women normally have low levels of testosterone. Boron had been withheld from their diets, and after continuing boron supplementation the concentration of testosterone did not further increase. All of these findings have little to do with athletes. Ferrando and Green⁵⁷ failed to find an effect of using boron supplements on bodybuilders' total testosterone, lean body mass, or strength. Current evidence suggests that boron supplementation has no anabolic effects.

Chromium has been promoted as an anabolic agent that will enhance energy metabolism, increase muscle, and decrease body fat. The popularity and claims for chromium picolinate stem from studies performed at Bemidji State University, but not published in peer-reviewed scientific literature.⁵⁸

A March 22, 1989 story in the *Los Angeles Times* quoted Evans as saying that "a new form of chromium could offer athletes an alternative to anabolic steroids, enable those with diabetes to use less insulin and cut cholesterol." At that point chromium picolinate became a popular product. The "health food" stores featured chromium and zinc picolinate as part of weight loss products and sports nutrition products.

In the scientific literature, it has been proposed that athletes have a higher dietary requirement for chromium due to documented chromium losses and a possible marginal chromium intake.⁵⁹ Acute exercise can increase urinary excretion of chromium^{60,61} and may alter chromium status in trained athletes.⁶² The total daily urinary chromium levels in nine runners was two times greater on an exercise day versus a non-exercise day.⁵⁶ The mean chromium intake for those consuming self-selected diets for seven days was well below the estimated safe and adequate intake (ESAI) of 50–200 $\mu\text{g}/\text{day}$.⁶³ It should be noted that the ESAI figures are estimates, and that this study was done on only nine athletes.

It is premature to recommend supplements such as chromium picolinate. The safety of chromium picolinate needs to be documented. Use of picolinic acid has resulted in physiological disorders while use of large doses could result in suboptimal iron status.⁵⁴ There is little evidence in peer-reviewed journals to indicate that chromium picolinate has any anabolic effects. Further research is needed to evaluate the physiological effects of other supplemental chromium compounds on chromium nutritional status and performance.

CONCLUSIONS

The term "buyer beware" is not strong enough when considering supplements for athletes. At present, the manufacturers have all the advantages. Their products do not have to be safe or effective, but Americans tend to believe that products on the market have been researched, tested, and inspected. American athletes, and the public, are being bilked out of millions of dollars which would be better spent on food. They believe, trust, and spend their money. Fortunately, most of these products will not be harmful, but most have never been scientifically proven to build muscle or meet other claims made by the manufacturers. The program manager for the Federal Trade Commission is quoted as saying "I'm sure they (sports nutrition supplements) are all fraudulent, but we don't have the time or money to go after all of them."¹⁴ Let us hope that the loopholes in the laws are soon plugged. It is difficult to combat such powerful multibillion dollar businesses who certainly do not want informed consumers. It is essential for correct nutrition information to reach the public. At the very least, physicians should ask their athletic patients about supplement use. Legitimate health professionals need to react. Why are so many worthless, if not harmful, supplements permitted to be advertised and sold?

Acknowledgments. The authors would like to thank Lois Myer (FDA Public Affairs Specialist), David Lightsey (Coordinator, Task Force on Ergogenic Aids National Council Against Health Fraud), and Peter Lemon, PhD, Kent State University, for so kindly providing current information.

REFERENCES

1. Williams MH: Ergogenic aids and ergolytic substances. *Med Sci Sports Exerc* 1992; 24:S344–348.
2. Schultz HW: *Food Law Handbook*. Westport, CT, The AVI Publishing Co, 1981, p496.
3. Pub. L 94–278, 501(a) which added 411 to the Federal Food, Drug, and Cosmetic Act.
4. Dykstra G: FDA and dietary supplement regulation. Presented by the Deputy Associate Commissioner for Regulatory Affairs by video link to the National Foods Association. Nashville, TN, July 27, 1992.
5. Council on Practice, The American Dietetic Association, 216 W Jackson Blvd, Chicago, IL 60606–6995.
6. Storlie J: Nutrition assessment of athletes: a model for integrating nutrition and physical performance indicators. *Int J Spts Nutr* 1991; 1:192.
7. Short SH: Dietary surveys and nutrition knowledge, in Hickson JF, Wolinsky I (eds): *Nutrition in Exercise and Sport*, Boca Raton, FL, CRC Press, 1989, pp309–344.
8. Philen RM, Ortiz DI, Auerback SB, et al: Survey of advertising for nutritional supplements in health and bodybuilding magazines. *JAMA* 1991; 268: 1008–1011.
9. Cowart VS: Dietary supplements: alternatives to anabolic steroids? *Phys Sports Med* 1992; 20:189–198.
10. Lightsey DM, Attaway JR: Deceptive tactics used in marketing purported ergogenic aids. *NSCA J* 1992; 14:26–31.
11. Marquart LF, Sobal J: Vitamin/mineral supplement use among athletes. *J Am Diet Assoc* 1992;A:56.
12. Short SH: Surveys of dietary intake and nutrition knowledge of athletes and their coaches, in Wolinsky I, Hickson JF (eds): *Nutrition in exercise and sport* ed 2. Boca Raton, FL, CRC Press, Inc, 1993 (in press).
13. Parr RB, Porter MA, Hodgson SC: Nutrition knowledge of coaches, trainers, and athletes. *Phys Sports Med* 1984; 12:127–138.

14. New York City Department of Consumer Affairs: *Magic Muscle Pills! Health and Fitness Quackery in Nutrition Supplements*. New York, May, 1992.
15. Committee on Diet and Health: *Diet and Health, Implications for Reducing Chronic Disease Risk*. Washington, DC, National Academy Press, 1989, p17.
16. Harper AE: Nutrition insurance—a skeptical view. *Nutrition Forum* 1987; 4:33–37.
17. Moss AJ, Levy AS, Kim I, et al: Use of vitamin and mineral supplements in the United States: current users, types of products and nutrients. *Advance Data no. 174* Hyattsville, MD, National Center for Health Statistics, 1989.
18. Anon: AE: Nutrition insurance—a skeptical view. *Nutrition Forum* 1990; 48:161–162.
19. Ink SL: Evaluating nutrition research, presented at the Food Health Claims Symposium, sponsored by Tufts University and the Food and Drug Administration, March 29, 1990, Boston, MA.
20. Williams MH: *Nutrition for Fitness and Sports* ed 3. Dubuque, IA, William Brown Publishers, 1992, p155.
21. Haymes EM: Vitamin and mineral supplementation to athletes. *Int J Sports Nutr* 1991; 1:146–169.
22. Van Der Beek EJ: Vitamin supplementation and physical exercise performance. *J Sports Sci* 1991; 9:77–89.
23. Clarkson PM: Vitamins and trace minerals, in Lamb Dr, Williams MH (eds): *Perspectives in Exercise Science and Sports Medicine, vol 4—Ergogenics—Enhancement of Performance in Exercise and Sport*. Ann Arbor, MI, William Brown Publishers, 1991, pp123–182.
24. Clarkson PM: Minerals: exercise performance and supplementation in athletes. *J Sports Sci* 1991; 9:91–116.
25. Weight LM, Noakes TD, Labadarios D: Vitamin and mineral status of trained athletes including the effects of supplementation. *Am J Clin Nutr* 1988; 47:186–191.
26. Barnett DW, Conlee RK: The effects of a commercial dietary supplement on human performance. *Am J Clin Nutr* 1984; 40:586–590.
27. Guillard J, Penaranda T, Gallet C, et al: Vitamin status of young athletes including the effects of supplementation. *Med Sci Sports Exerc* 1989; 21: 441–449.
28. Coburn SP, Ziegler PJ, Costill DL, et al: Response of vitamin B-6 content of muscle to changes in vitamin B-6 intake in men. *Am J Clin Nutr* 1991; 53:1436–1442.
29. Schaumburg H, Kaplan J, Windebank A, et al: Sensory neuropathy from pyridoxine abuse. *N Engl J Med* 1983; 309:445–448.
30. Williams MH: Nutritional ergogenic aids and athletic performance. *Nutrition Today* 1989; 7–14.
31. Grandjean AC, Hursh LM, Majure WC, et al: Nutrition knowledge and practices of college athletes. *Med Sci Sports Exerc* 1981; 13:82.
32. Krowchuk DP, Anglin TM, Goodfellow DB, et al: High school athletes and the use of ergogenic aids. *Am J Diseases of Child* 1989; 143:486–489.
33. Parr RB, Porter MA, Hodgson SC, et al: Nutrition knowledge and practice of coaches, trainers, and athletes. *Phys Sports Med* 1984; 12:127–138.
34. Douglas PD, Douglas JG: Nutrition knowledge and food practices of high school athletes. *J Am Diet Assoc* 1984; 84:1198–1202.
35. Barrett S: Dietary supplement frauds deserve greater FDA priority. *Priorities*. American Council on Science and Health, New York, NY 1992; Winter, 7–10.
36. Carthart EP: Influence of muscle work on protein metabolism. *Physiol Rev* 1925; 5:225–243.
37. Lemon PWR: Effect of exercise on protein requirements. *J Sports Sci* 1991; 9:53–70.
38. Meredith CN, Zackin MJ, Frontera WR, et al: Dietary protein requirements and body protein metabolism in endurance-trained men. *J Appl Physiol* 1989; 66:2850–2856.
39. Freidman JE, Lemon PWR: Effect of chronic endurance exercise on retention of dietary protein. *Int J Sports Med* 1989; 10:118–123.
40. Tarnopolsky MA, MacDougall JD, Atkinson SA: Influence of protein intake and training status on nitrogen balance and lean body mass. *J Appl Physiol* 1988; 64:87–193.
41. Walberg JL, Leidy MK, Sturgill DJ, et al: Macronutrient content of a hypoenery diet affects nitrogen retention and muscle function in weight lifters. *Int J Sports Med* 1988; 9:261–266.
42. Lemon PWR: Nutritional factors in strength and endurance training. *Med Sports Sci* (in press).
43. Short SH, Short WR: Four-year study of university athletes' dietary intake. *J Am Diet Assoc* 1983; 82:632–645.
44. Knopf RF, Conn JW, Fajans SS, et al: Plasma growth hormone responses to intravenous administration of amino acids. *J Clin Endocrinol Metab* 1965; 25:1140–1144.
45. Lemon PWR: Protein and amino acid needs of the strength athlete. *Int J Sport Nutr* 1991; 1:127–145.
46. Jacobson BI: Effect of amino acids on growth hormone release. *Phys Sports Med* 1990; 18:63–70.
47. Williams MH: *Nutrition for Fitness and Sport* 3 ed. Dubuque, IA, Wm C Brown, 1992, p125.
48. Harper AE, Benevenga NJ, Wohlheuter RM: Effects of ingestion of disproportionate amounts of amino acids. *Physiol Rev* 1970; 50:428–557.
49. Benevenga NJ, Steele RD: Adverse effects of excessive consumption of amino acids. *Ann Rev Nutr* 1984; 4:157–181.
50. Howe WB: Ground up beef testicle, in scanning sports. *Phys Sportsmed* 1989; 17:45.
51. Friedl KE, Moore RJ, Marchitelli LJ: Steroid replacers: let the athlete beware. *NSCA J* 1992; 14:14–19.
52. Palamalai B, Hejtmancik E, Bridges CH, et al: The isolation and identification of steroidal sapogenins in Kleingrass. *Vet Hum Toxicol* 1990; 32: 314–318,52,52.
53. Wheeler KB, Garleb KA: Gamma-oryzanol-plant sterol supplementation: metabolic, endocrine, and physiologic effects. *Int J Sports Nutr* 1991; 1:170–177.
54. National Research Council: *Recommended Dietary Allowances* 10th ed Washington, DC, National Academy Press, 1989, pp176, 267.
55. Hunt CD, Shuler TR, Mullen LM: Concentration of boron and other elements in human foods and personal-care products. *J Am Diet Assoc* 1991; 91: 558–568.
56. Nielsen FH: Facts and fallacies about boron. *Nutrition Today* 1992; 27 (no 3):6–12.
57. Ferrando A, Green NR: The effect of boron supplementation on lean body mass, plasma testosterone levels and strength in male weightlifters. *FASEB J* 1992; 6:A1946.
58. Moore RJ, Friedl KE: Physiology of nutritional supplements: chromium picolinate and vanadyl sulfate. *NSCA J* 1992; 14:47–51.
59. Lefavi RG, Anderson RA, Keith RE, et al: Efficacy of chromium supplementation in athletes: emphasis on anabolism. *Int J Sports Nutr* 1992; 2: 111–122.
60. Anderson RA, Bryden NA, Polansky MM, et al: Exercise effects on chromium excretion of trained and untrained men consuming a constant diet. *J Appl Phys* 1988; 64:249–252.
61. Anderson RA, Polansky MM, Bryden NA, et al: Effects of exercise (running) on serum glucose, insulin, glucagon, and chromium excretion. *Diabetes* 1982; 31:212–216.
62. Campbell WW, Anderson RA: Effects of aerobic exercise on the trace minerals chromium, zinc, and copper. *Sports Med* 1987; 4:9–18.
63. Anderson RA, Kozlovsky AS: Chromium intake, absorption, and excretion of subjects consuming self-selected diets. *Am J Clin Nur* 1985; 41:1177–1183.

The role of physicians in dental quackery

JOHN E. DODES, DDS, MARVIN J. SCHISSEL, DDS

Dentistry is beset with problems, not the least of which is the growing popularity of "alternative" methods, eagerly accepted by patients and lucrative to the practitioner, but unscientific and potentially dangerous. They amount to quackery.¹ More and more we are encountering instances of patients whose physicians, unacquainted with the dubious status of these "alternative" methods and misinformed by anecdotes or media hype, have been referring patients with chronic pain and puzzling malaise to dentists for these

treatments. This article is intended to familiarize physicians with these dubious procedures so that more care will be taken with referrals to dentists. While some physicians may actually subscribe to these bizarre "alternative" theories, we suspect that most physicians referring for these therapies have trustingly accepted the misinformation they have heard from these dentists or from the media. Regardless of the physician's motive, it is still the patient who suffers.

The management of chronic pain and malaise of elusive etiology can be frustrating. Dealing with these patients is often time-consuming and aggravating. Physicians confronted with such a patient and unable to develop a

Address correspondence to Dr Dodes, Woodhaven Dental Associates, PC, 86-39 Woodhaven Blvd, Woodhaven, NY 11421.

reasonable diagnosis might well look favorably on a dentist who, claiming to have answers to the dilemma, will take the troublesome patient off his/her hands. Most referrals to dentists for chronic non-dental pain or malaise fall into one of two categories: temporomandibular joint disorders (TMJD) or mercury toxicity.

TEMPOROMANDIBULAR JOINT DISORDERS

Patients with chronic pain of the head, neck, back, and legs, with headaches, tinnitus, and even menstrual problems, and other vague symptoms difficult to diagnose might be referred to a TMJD specialist. Often the referring physician is an otolaryngologist or internist, acting on the mistaken belief that vague ear pain might be related to the temporomandibular joint (TMJ), and in the equally mistaken belief that the "TMJ specialist" can successfully treat it.

There is no recognized specialty in TMJ. However, too often the self-proclaimed TMJ specialist uses unproven or disproven methods. Diagnosis may be based on the quack notion of "applied kinesiology,"^{2,3} or on the use of electronic devices which have been shown to be unreliable diagnostically and without therapeutic effect. Some of these unproven electronic methods include electromyography (EMG), jaw tracking, silent period durations, thermography, sonography, and Doppler ultrasound.⁴ Treatment, usually based on the long discredited theory that a "bad bite" is the cause of these symptoms, has included "improving the bite" by extensive adjusting and reshaping the teeth or making elaborate permanent or removable prosthetic devices, or even by surgery on the jaws or the TMJ. These treatments are invasive, can be disastrous to the long-term health of the mouth, and in common with other quack treatments, are not supported by either scientific data or investigations. Some 90% of patients with these symptoms will improve if left alone or if conservatively treated with anti-inflammatory drugs, moist heat, and simple jaw exercises.⁵⁻⁸

It is true that there are some dentists who treat this type of pain legitimately and who do provide valid diagnostic and therapeutic services; not every dentist in this field is a quack. In addition, there are occasions when non-invasive appliances can be appropriately used, often as placebos, and on extremely rare occasions surgery is justified. However, these are exceptions. Unfortunately, too many TMJ practitioners are of the unscientific stripe, and physicians must remember that every undiagnosed facial or body pain is not a TMJ problem, and is not a reason for referral. Only pain relating to jaw excursions might mean a legitimate TMJ problem. Most facial pain and virtually all body pain is unrelated to the TMJ.

MERCURY TOXICITY

Silver amalgam fillings are about 50% mercury, and some dentists, without scientific support, are blaming a host of diseases on the minuscule amount of mercury which allegedly leaks out of amalgam fillings. Among these ailments are multiple sclerosis, Parkinson's disease, immunodeficiency diseases, and emotional problems. The anti-amalgam quacks assert that all amalgam fillings must be removed, sometimes in a specific order according to their electric "polarity," and that "chelating agents" be used to "detoxify" the body of mercury. Unreliable devices such as "Dermatron," "Amalgameter," and the Jerome Mercury detector have been used for diagnosis.⁹

The unnecessary removal of silver-amalgam fillings from a mouth can be a mutilating and dentally crippling procedure. A

number of successful malpractice actions have been brought against dentists as a result of this treatment. The American Dental Association Council has declared such treatment to be "improper and unethical."¹⁰ However, the press and media, finding the false assertions of the anti-amalgam forces irresistible, have acted to powerfully reinforce these quack notions about amalgam toxicity in the minds of the public. We suspect that many health professionals have been similarly misinformed, particularly those who look more to the media than to refereed journals for their information.

The astute reader will recognize that the conditions treated by TMJ and anti-amalgam dentists are those featuring chronic, difficult-to-diagnose pain, vague malaise, or progressive, variable-rate physical degeneration. We call these the "quack sensitive" ailments, the very complaints which quacks are eager to treat. In these conditions, symptoms wax and wane, emotional factors play a confounding role, and current medical practice is unable to offer cures or, sometimes, even encouragement. This environment provides a fertile field for the fraudulent promises and treatment excesses of quackery.

The following incident provoked us to write this article: Recently a dentist who specializes in oral surgery asked for our advice. He had performed an apicoectomy and placed a retrograde silver-amalgam filling in the root apex. This is a common and appropriate procedure. However, when the patient learned that an amalgam filling was used he was alarmed, because he had heard and believed the unfounded claim that amalgam fillings were dangerous. His fears were aggravated by a "holistic" physician who, citing a misinformed segment of a television show as his authority, told him that his symptoms were probably caused by the amalgam. This physician demanded that the dentist remove the amalgam. This would have required additional and unnecessary surgery with considerable trauma and increased risk to the patient. The surgeon of course refused, and the physician referred the patient to another dentist who extracted the tooth.

We have seen patients and have heard reports of many other patients who have been mistreated by dental quacks. Some physicians, however inadvertently, have been contributing to the spread of dental fraud by poorly informed referrals to pseudoscientific dentists. We urge physicians to evaluate your dental colleagues and their claims as critically and carefully as you evaluate your medical referrals.

REFERENCES

1. Berry JH: Questionable care: what can be done about dental quackery? *JADA* 1987; 115:679-685
2. Friedman MH: Applied kinesiology—double-blind pilot study. *JADA* 1981; 45:321-323
3. Vates JW, Koen TJ, Semenick DM, et al: Effect of a mandibular orthopedic repositioning appliance on muscular strength. *JADA* 1984; 108:331-337
4. Mohl ND, Ohrbach RK, Crow HC: Devices for the diagnosis and treatment of temporomandibular disorders. *J Prosthetic Dent* 1990; 63:198-201, 332-335, 472-476.
5. Clarke NG: Occlusion and myofascial pain dysfunction: is there a relationship? *JADA* 1982; 104:443-446
6. Greene CS, Laskin DM: Long term evaluation of treatment for myofascial pain dysfunction syndrome: a comparative analysis. *JADA* 1983; 107:235-238
7. Okeson JP, Hayes DK: Long term results of treatment for temporomandibular disorders: an evaluation by patients. *JADA* 1986; 112:473-478
8. Greene CS, Marbach JJ: Epidemiologic studies of mandibular dysfunction: a critical review. *J Pros Dent* 1982; 48:184-190.
9. Dodes JE: Amalgam toxicity—A review of the literature. *J Operative Dent* 1988; 13:32-36.
10. ADA Principles of Ethics and Code of Professional Conduct. Advisory Opinion 7, Section 1-J. Res 42H-1986; 536.

Reflections on the use of unproven arthritis remedies

JAMES M. STROSBURG, MD

It is not surprising that over \$3 billion are spent annually for unproven arthritis treatments.¹ Over 40 million Americans are afflicted by our nation's number one chronic crippling illness and most have symptoms every day of their lives.² According to the Arthritis Foundation, arthritis quackery succeeds because of a widespread lack of understanding about arthritis, the absence of a cure at present, the tremendous pain associated with the disease and the fact that there are so many people suffering that promoters have a huge market. The symptoms of arthritis come and go like the tide, allowing people to connect the disappearance with a phony remedy they have been taking.³

This essay does not attempt to review the hundreds of useless treatments which have been promoted to help arthritis patients. This information is readily available at the 75 chapter offices of the Arthritis Foundation throughout the country and in the Foundation's book, *Unproven Remedies Resource Manual*. The latter is a catalogue of non-orthodox treatments which have been used by patients throughout recent years. These include alternative healing philosophies such as homeopathy and naturopathy; special diets such as elimination diets and fasting; nutritional supplements including amino acids, mega-vitamin therapy and selenium; herbal remedies including alfalfa, garlic, and kelp; procedures such as colon cleansing; diagnostic tests including hair analysis and miscellaneous treatments such as copper bracelets and snake oil. They vary from relatively harmless to potentially dangerous. Over 300 entities are discussed in this reference book with respect to therapeutic claims, adverse reactions, and scientific studies. A list of references is included under each treatment.¹

"Unproven" or "non-orthodox" indicates that scientific studies are lacking to validate or substantiate therapeutic claims. "Quackery" or "fraud" indicates deliberate attempts to misrepresent.

It behooves a physician treating an arthritis patient to inquire about the use of alternative treatments and to become knowledgeable about any possible harmful effects of these claims for which he is taking these treatment.

CASE REPORT

A 62-year-old college educated woman suffered from rheumatoid arthritis since the age of 20. Before her husband's death three years previously, she received treatment at some of the most prestigious medical centers and clinics in the Northeast. She had received gold, hydroxychloroquine sulfate, intra-articular injections of cortisone, physical and occupational therapy, and multiple anti-inflammatory drugs. She had many complications including rashes,

peptic ulcer disease, thinning of her skin with multiple ecchymoses, and cataracts. At the time of her husband's death, she suffered from flexion contracture of her hips and knees which confined her to a wheelchair. Because of upper extremity deformities, she required assistance in dressing and toileting and employed a full-time health aide. She also suffered from anxiety and depression.

On the advice of a well-meaning friend, she traveled to a clinic in rural Mexico to receive what she was told was dimethylsulfoxide (DMSO). She was there for three days and received an intravenous medication and a large supply of pills to take daily for three months. On returning home, she felt like her disease had finally gone into remission. Her pain and stiffness decreased, and she was able to perform many of her activities of daily living.

About one month after her return, she developed melena and visited her internist who noted that she had developed signs of Cushing's syndrome. On analysis, the pills were found to be prednisone. She was admitted to a hospital for further diagnosis, treatment, and rehabilitation.

DISCUSSION

It is easy to empathize with this patient and it is easy to understand her frustration with a life of pain and disability. Her doctors did not know the cause of her rheumatoid arthritis. Numerous drugs resulted mostly in side effects rather than symptom relief. Her pain got progressively worse and her joints became more deformed. It is understandable that she was desperate and jumped at the opportunity to be cured.

In my experience, neither the educational level nor the native intelligence of patients protect them from the temptations of unproven remedies. The force of human nature, in its quest for symptom relief, overpowers the intellect.

I once treated on the same day two 50-year-old men, both engineers working in middle management, who had rheumatoid arthritis of remarkable similar severity. Both experienced several hours of pain and morning stiffness. Their joints had a comparable degree of synovitis. They both were anemic and had elevated sedimentation rates. Their radiographs showed similar erosions. They in fact were almost rheumatologic identical twins.

The first man boasted, "Doctor, I am doing great! I was able to play nine holes of golf for the first time in two years! I took the golf cart and the pain was so slight that after 12 aspirin tablets I felt comfortable! It was great!"

The second man complained, "Doctor, I am doing terribly! I tried to play golf for the first time in two years, but I had to take a golf cart. I had to quit after nine holes, the pain was so bad. I needed 12 aspirin tablets to feel comfortable."

Address correspondence to Dr Strosberg, Chief of the Medical Dental Staff, Sunnyview Rehabilitation Hospital, 1270 Belmont Ave, Schenectady, NY 12308.

The second patient is a potential victim of arthritis fraud. He is "doing terribly." His physician needs to educate him about his disease. He must be questioned at each visit about non-prescribed treatments, and his doctor must become knowledgeable about such treatments to watch for side effects.

The ultimate barrier to consumer use of unproven remedies is the total doctor patient relationship. This may not be achievable with some patients who may be unable to develop trust in their physician. To decrease the possibility that our patients will resort to unproven methods, we must make them feel confident that everything scientifically possible is being done to treat their illness. To achieve this, we physicians must communicate both empathy and competence. Rheumatologists being specialists, may sometimes elicit an extra "placebo effect."

A necessary ally to the doctor-patient relationship is patient education. Physicians probably overestimate the sophistication of their patients' understanding of their illness. A telephone survey of a random sampling of 300 respondents indicated the poor level of public knowledge on the causes of arthritis.⁴ Half of those questioned believed that arthritis can be caused by poor diet and cold or wet climates. Bee venom, vitamins, copper bracelets, special diets, and DMSO were accepted as treatments by more than half. It is important to note that 41% of the respondents had post-high-school education.⁴

There is an analogy between our nation's war on drugs and war on medical fraud. It is very difficult, if not impossible to eliminate the source of illegal or unproven substances. The number of people at risk is extremely large. The most viable solution, in my opinion, is education, both public education in the form of media presentations on the most common and dangerous non proven remedies, and personal one on one education, by the physician, targeted for those of his patients who are at the highest risk.

To assist doctors in educating their patients, the Arthritis

Foundation produces hundreds of booklets on all aspects of rheumatic diseases and treatments. There is even a pamphlet on unproven remedies. This large body of literature is available for physicians waiting rooms and to individual patients from Chapter offices.

What about the chicken soup analogy? Most agree that this traditional remedy can not hurt and that maybe it can help. Some might say the same for copper bracelets. The concern is that when a patient has symptoms and uses an unproven remedy, he may be delaying effective treatment. An example would be the use of a copper bracelet for a septic arthritis when the joint can be destroyed in a short period of time. Obviously using unproven remedies for chest pain, could even have a more serious result.

Another argument against the chicken soup treatment is that some patients, depending on their diagnosis, may temporarily improve during the unproven treatment. This may be because of a natural remission in the disease (placebo induced or otherwise), or it may be because the symptoms would be intermittent anyway, such as muscle spasm pain of fibrositis. The end result is more "converts" to the "copper bracelet," who will promote this treatment to their friends with rheumatoid arthritis and thus discouraging them from seeking medical care. In conclusion, although unproven remedies will always be available, there is much we as physicians can do to protect our patients.

REFERENCES

1. The Arthritis Foundation: *Unproven Remedies Resource Manual*, Atlanta, GA, 1990, p1.
2. US Department of Health and Human Services: *Health Information and the use of Questionable Treatments*, Study N:833015, Louis Harris and Assoc, Sept 1987, p184.
3. *Quackery, a Ten Billion Dollar Scandal*, A Report by the Chairman of the Subcommittee on Health and Long Term Care of the Select Committee on Aging, House of Representatives, 98th Congr, 2nd Sess, Committee Publ No98.435, Washington, DC, May 1984, US Government Printing Office.
4. Price JH, Hillman KS, Toral ME, et al: The public's perceptions and misperceptions of arthritis. *Arthritis Rheum* 1983; 26:1023-1028.

Remedies for a society's debilities

Medicines for neurasthenia in Victorian America

JOHN STEA, MD, WILLIAM FRIED, PhD

George Miller Beard wrote in 1880, that "not only for the relief of pain, but for the relief of exhaustion, deeper and more distressing than pain, do both men and women resort to the drug shop. . . ."¹ (Fig 1). Neurasthenia, commonly termed nervous exhaustion in Victorian America, was viewed by George Beard, a New York City neurologist and prolific writer on the topic, as predominantly an American phenomenon that had arisen from the "fatiguing" effects of an increasingly urbanized society. Encompassing a wide range of symptoms, including malaise, depression, insomnia, and indigestion or dyspepsia, the diagnosis gained in popularity with both physicians and the general public as the 19th century unfolded. Those professionals who were diagnosing and treating neurasthenia, neurologists, general practitioners, gynecologists, and alienists (physicians who primarily treated the insane), offered an almost endless variety of treatment regimens, including "rest cures," special diets, "electrotherapy," and medicines.² The medicines used for neurasthenia between the years 1869, when George Beard's first paper on the topic appeared, and the first decade of the 20th century, were a broad range of substances, from atropine to zinc oxide. Medical journals became replete with advertisements for commercial medicines that were said to be of benefit for neurasthenia or nervous exhaustion. In their endless quest for alleviation of the debilitating symptoms, however, many individuals placed their trust in the inexhaustible supply of patent medications. In an era of minimal regulation, there was no clear distinction between standard medicines for treatment and the patent medicines. The picture was further blurred by the lack of specificity in the approaches to treatment in the case of neurasthenia. The wide gamut of substances available for neurasthenias throughout the latter decades of the 19th century was used to fill a therapeutic vacuum created by the dearth of effective, scientifically proven psychopharmacological and psychological therapies.

It is not unusual for patients with symptoms of anxiety and depression to describe their experiences as "nerves" or "nervousness." Nineteenth century writers on neurasthenia ascribed psychological symptoms to somatic causes. Allusions to neurasthenia appeared in a number of popular journals, household "medical advisors" and medical advertisements, encouraging the Victorian public to biologize aspects of mental disorders. The importance of neurasthenia lies in its timelessness, as modern conditions such as chronic fatigue syndrome are comparable.³ These diagnos-

tic labels confer respectability on sufferers by imputing a biological rather than psychological origin to their complaints. Cultural issues such as changes in gender roles are a significant sub-text in the study of neurasthenia, making it even more relevant for contemporary historians.

George Beard observed in his book, *Treatise on Nervous Exhaustion*, published in 1880, that neurasthenia was a common condition that had acquired a number of designations. He wrote the following:

In spite of its frequency and importance, neurasthenia although long recognized, in a vague way among the people and the profession under such terms as "general debility," "nervous prostration," "nervous debility," "nervous asthenia," "spinal weakness" and more accurately, by some of its special symptoms and accompaniments, as "spinal irritation," "nervous dyspepsia," "oxaluria," "cerebral and spinal anaemia," and "hyperaemia," is even now but just beginning to find recognition in the literature of nervous diseases.^{1(p49)}

Among the myriad symptoms that were observed by physicians treating these disorders, the central feature was prostration or general weakness. E. H. Van Deusen, medical superintendent of the Michigan Asylum for the Insane, recognized "malaise," as a leading symptom, followed by "impaired nutrition and assimilation, muscular atonicity, changing the expression of the countenance, uterine displacements. . ." together with " . . . irritability, mental depression, impaired intellectuation, melancholia and mania."⁴ Beard, who had worked with Thomas A. Edison, evoked the analogy of dimmed lights, resulting from an overloaded dynamo, to explain the diminution of energy described in neurasthenia.⁵ Drawing on the work of the scientist Du Bois-Reymond, Beard postulated that the nervous system itself underwent molecular changes, becoming "dephosphoralized" from its use, resulting in changes that inevitably impaired the brain in those who were vulnerable.⁶ Undoubtedly influenced by the works of Charles Darwin, Beard also stressed the role of heredity in the etiology of neurasthenia. He described the "nervous diathesis," or "tendency of the constitution for nervous disease," including "nervous debility." Characterized as "strongly hereditary," Beard suggested that these conditions "may run in families for many generations."⁷ Abbey and Garfinkel attribute Beard's argument that the higher classes were predisposed to neurasthenia because of their presumably more highly evolved nervous system to his belief in social Darwinism.³ This presumably advanced nervous system was thought to be vulnerable to the stressful conditions of modern civilization. Beard argued that it was the duty of the psychologist to study the effects of those stressors on the human nervous system.⁸

From the Department of Psychiatry, Maimonides Medical Center, Brooklyn, NY.

Address correspondence to Dr Stea, Department of Medicine, Maimonides Medical Center, 4802 Tenth Avenue, Brooklyn, NY 11219.



FIGURE 1. George Miller Beard (courtesy of The New York Academy of Medicine).

The role of diet and nutrition was often a central concern of physicians whose treatment of neurasthenia took into consideration the production of toxic substances that they thought were deleterious to the nervous network. Edward Cowles, a Massachusetts neurologist, in pointing out revelations in the field of bacteriology, added the following in 1891:

Thus it comes to be a part of the clinical problem in mental disorders to consider whether the overworked brain may not only have its nutrition, and functional activity, diminished by imperfect removal of waste products, but that further poisoning of its cells and fibers may come from toxic substances in the circulation, due to imperfect digestion and assimilation.⁹

Beard emphasized the importance of the “digestive apparatus,” as one segment of a reflex arc, including the “stomach” and the “reproductive system.”⁸(pp251,252) Although this concept was a reflection of the frequent association between neurasthenia and dyspepsia or nervous indigestion, it also suggested a relationship to sexual physiology and behavior, including masturbation. Known commonly as “self abuse,” masturbation as a putative etiological factor for neurasthenia was examined by Collins and Phillips, of the New York Graduate School in 1899. They stated that “masturbation, (under which we included for convenience sake other irregular forms of sexual indulgence), is generally recognized as being very important,” reflecting the contemporary notion that this sexual activity drained the nerve force of men.¹⁰ Many writers on neurasthenia, including George Beard, believed that women were especially vulnerable to this condition, a view that was also held by many physicians, during the era. Many thought that nervous prostration in women arose from “female weakness” or uterine abnormalities. Beard stated in one work published in 1878, that women “. . . seem to have more sickness, certainly more of diseases of debility and exhaustion.”⁷(pp138,139) In his work on sexual neurasthenia, Beard pointed to a contrast between “the Indian squaw,”

who “keeps most of her nerve force,” and the “sensitive white women. . . who can never hold a powerful reserve, but must live and does live, in a physical sense, from hand to mouth. . . .”¹¹ In her article, *The Fashionable Diseases: Women's Complaints and their Treatment in Nineteenth-Century America*, Anne Douglas Wood concluded that the general ill health of women described by many practitioners during the Victorian age had become “positively fashionable.” She added that the special focus on the uterus by 19th century physicians led them to attribute many diseases, including nervous prostration, to the womb.¹² Haller, however, pointed out that not all writers on neurasthenia attributed nervous weakness in women to the taxing of a vulnerable system. The neurologist Charles Dana, for example, thought that idleness not overwork produced neurasthenia in women.¹³ In contrast with the notion that the overly crowded schedule of the urban worker produced nervous exhaustion, Van Deusen focused on the “early married life” of farmer’s wives as a predisposing condition, stating:

The urgency of farm work necessitates hurried, unsocial meals, and as night closes in, wearied with his exertions, the farmer is often accustomed to seek his bed at an early hour, leaving his wife to pass the long and lonely evening with her needle. Whilst the disposal of his crop, and the constant changes in the character of farm labor afford her husband sufficient variety and recreation, her daily life and especially if she had also the unaided care of one of two ailing children, is exhausting and depressing to a degree of which but few are likely to form any correct conception. From this class come many applications for the admission of female patients.⁴(p447)

Although physicians ascribed neurasthenia primarily to an enfeebled constitution resulting from a loss of nerve force and a pathological condition of the internal organs, they also conceded the importance of environmental factors in its etiology. A common motif was that the business activity of the urban professional or “brain-worker” consumed the nerve force with which he had been endowed. In addition to “domestic trouble,” “prolonged anxiety,” and “pecuniary embarrassment, leading to nervous exhaustion,” Van Deusen’s list of predisposing factors also included “prolonged exposure to a malarial region.”¹⁴(pp445,446) During the years before the infectiousness and transmissible nature of malaria were elucidated, the disease was often associated with nervous prostration both in etiology and treatment. Beard wrote, for example: “one of the great afflictions of America-malaria, often complicates neurasthenia; aggravates it, makes it harder to treat, masks and confuses its symptoms; and the two diseases not only exist together, but may be mistaken for each other.”

The treatment regimens for neurasthenia were a reflection of theories of the etiology of this condition. Therefore, the treatment of neurasthenia by 19th century physicians was designed to restore the depleted nerve force and help buttress the body’s natural healing processes. Rest cures, special diets, and medications that would stimulate the “system,” rid the body of “auto-toxic” substances, and procure rest through sedation, were used. Devices were constructed for the application of static electricity, thought to “re-charge” the body’s lost nerve force. Retreats were established in the outskirts of urban centers, serving as institutions of rest and relaxation. McComb, of the Emanuel Movement of Boston, offered relief for female sufferers of neurasthenia, through work in the ministry.¹³(p481) Specific treatment for neurasthenia, such as drug choice, was influenced by various schools of thought to which practitio-

ners belonged. Gossling pointed out that the majority of physicians who wrote on neurasthenia were regulars, a term used to describe those physicians subscribing to the traditional therapeutics taught at most medical schools. Other physicians who treated neurasthenia included the homeopaths who generally prescribed smaller doses of medications, and the botanics, who shunned mineral therapeutics such as mercury, and used compounds derived from plants. Electrotherapists, such as Margaret Cleaves of New York City, used devices constructed for the application of static electricity, thought to "recharge" the body's lost nerve force. Gossling emphasized that although a wide variety of clinicians offered different treatments for neurasthenia, the approach to this condition seemed to have been more dependent on the physicians' "collective gender" and class attitudes than on educational background or specialization.^{2(pp143-163)} Of the different treatments, medications played a major role in the treatment of neurasthenia during the years after the appearance of Beard's first paper on the subject in 1869.

PRESCRIPTION MEDICINE FOR NEURASTHENIA

The long list of drugs used in physicians' prescriptions for the disorder included strychnine, phosphates, bromides, chloral hydrate, alcohol, cocaine, opium, cannabis, and cod liver oil. These were listed in the *United States Dispensatory* which, published since the 1830s, provided physicians with instructions for the preparation and administration of standard therapeutics. Prescriptions were either prepared by physicians themselves or at the pharmacy. Strychnine and its derivative, *nux vomica*, were recognized as stimulants in small doses and poisons in larger ones. Derived from the plant *Strychnos nux vomica*, its use was described by E. H. Van Deusen for one case in 1869: "...in the case of a female treated here, a moderate dose of the medication in the evening, followed by a second early in the morning, invariably afforded pleasant relief a few hours afterwards."^{4(p460)} Collins and Phillips described that in addition to its "tonifying effect, particularly on the muscular system," strychnine "frequently restores the appetite as does arsenic or quinine."^{10(p421)} Commonly known as Peruvian Bark, quinine was derived from several species of the cinchona tree on the western coast of South America and had been used since 1688 for intermittent fevers or agues.¹⁴ This medicine was ranked "first as a nerve tonic" by Van Deusen, who administered it in dilute phosphoric acid, and he found it especially useful in "cases marked by considerable irritability with emaciation."^{4(p459)} Tonics were considered substances that fortified the system with a cumulative physiological effect, the increments of which were barely perceptible. Similar to tonics, alteratives were thought to gradually reestablish health with little conspicuous effect. Arsenic was widely used as a tonic and alterative for the treatment of nervous prostration. It was one ingredient of a prescription for a "nerve tonic and sedative" for neurasthenia, along with "coca and citric acid" in 1900.¹⁵ Other alteratives employed as stimulants to counteract neurasthenia were some ammonia preparations including bromide of ammonia salt.

Two other important tonics for neurasthenia were iron and zinc. Recommended by the Dispensatory to "improve the quality of blood" and recognized as an "essential constituent of the red corpuscle," iron was specified in many prescriptions for neurasthenia. . . .¹⁶ These included treatments for what were considered localized conditions

-ADVERTISEMENT-

Exhaustion

Horsford's Acid Phosphate

Overworked men and women, the nervous, weak and debilitated, will find in the Acid Phosphate a most agreeable, grateful and harmless stimulant, giving renewed strength and vigor to the entire system.

Dr. Edwin F. Vose, Portland, Me., says: "I have used it in my own case when suffering from nervous exhaustion, with gratifying results. I have prescribed it for many of the various forms of nervous debility, and it has never failed to do good."

FIGURE 2. A popular medicine for neurasthenia that contained phosphorus (*Science*, 1897, vol 6, copyright American Association for the Advancement of Science).

such as the spinal anemias. George Beard described his use of the zinc preparations, "particularly the bromide, valeriante, and oxide," forms as "sedatives of very great value in various neurasthenias."^{1(p152)}

Phosphorus, the element that was observed to be a major component of the nerve cell, was ubiquitous in regimens for the treatment of neurasthenia (Fig 2). Judson B. Andrews, assistant physician in the New York State Lunatic Asylum, described in 1869 the application of dilute phosphoric acid as being a useful tonic for debility of the nervous system when mixed with substances that included "ammonia, glycerine and sherry wine."¹⁷ In 1876, Samuel R. Percy, also of New York, in a prize winning essay, described the injurious effect of phosphoric acid or free phosphorus, that included Bright's disease, a renal affliction. Percy urged that the oxides of phosphorus or hypophosphates were safer and applicable to nervous debility: in one experiment, he administered "hypophosphorus" to a dog, noting that "he was more boisterous in play" and that it acted as a "powerful aphrodisiac."¹⁸ One year later, Edward R. Squibb of Brooklyn, New York, recommended that phosphorus should be dissolved in cod liver oil, writing: "the more effective application seems to be to the functional derangements of the nervous system which are of an adynamic character, or where organic or structural changes are slight. . . ."¹⁹

Other stimulants in the physicians' armamentarium for neurasthenia included cocaine, cannabis, and caffeine. The 1870 *Dispensatory*, described how the South American natives obtained energy for a several days' journey by chewing the coca leaves, alleged to "support the strength for a considerable time in the absence of food."^{16(pp1,591;1,592)} George Beard employed cocaine as a stimulant for the

treatment of his patients, stating in 1880 that "it has, without doubt, a special and most interesting sustaining and tonic power." He also described *Cannabis indica*, as "one of the most trustworthy, most reliable and valuable of remedies," adding that it was beneficial in headache.^{1(p148-151)} Caffeine was often used in conjunction with ergot and belladonna to abate the headache of the neurasthenic. Alcohol, or *Spiritus fermenti*, long known for its stimulating properties, served as an ingredient in many prescriptions for neurasthenia, and Beard recommended wine, particularly claret and burgundy.^{1(p156)} J. Leslie Tobey, of Boston, Massachusetts, in his description of psychotherapeutics in 1887, cited a recommendation of Dr Sidney Ringer, for a "glass of bitter beer at meals" to assist "those living in the cities, whose brains are overtaxed, those having much brain work."²⁰

Insomnia was a major consideration in treating the neurasthenic and bromides, chloral hydrate and narcotics were among the popular sedatives employed. In his *Treatise on Nervous Prostration*, Beard compared the qualities of the bromides to those of "electricity and massage." He claimed that both "give rest by slowing down the nerve activity."^{1(p154)} Physicians treating neurasthenia employed a number of bromides, including salts of sodium, potassium, zinc ammonia, and lithium, often blending them with chloral hydrate. J. S. Greene recorded in the *Boston Medical Journal* of 1883:

A capacity for taking extra sleep is highly to be prized as a means towards restoration; but some there are who cannot attain it. If the effect of overstrain be heavily visited upon the brain, causing actual insomnia, restlessness, excitability, it is expedient to compel sleep and a dormant disposition by liberal doses of bromides, perhaps to some extent associated with chloral.²¹

Of ten case presentations for neurasthenia in 1872, T. W. Fisher, employed chloral hydrate in the treatment of six cases, and bromides in four others,²² Van Deusen found morphine useful for insomnia, as well as for pain in neurasthenias; he stated: "relief from intense pain to secure sleep and the strength of the patient, may be produced by the hypodermic use of the acetate of morphia which will generally be found successful." He added that "this with a carefully conducted course of nerve tonics, has in the cases coming under our observation, uniformly restored the patient to his previous health."^{4(p455)} Expressing his attitude toward the use of popular hypnotics, Beard stated, "...a remedy to be ranked with alcohol and opium is chloral, which is now greatly over-used. . . ." He added, "...indeed one of the first signs and proofs of good results of treatment of these cases is that they can dispense with their opium and alcohol or chloral."^{1(p154)}

Regulating the patient's nutrition was considered important in restoring his depleted energy reserve. Cod liver oil, alone or combined with phosphorus, was a common nutritive supplement. Urging that cod liver oil "...is not merely a nutritive agent. . .", the *Dispensatory* stated that "...in consequence of some peculiar principle or principles it contains it exercises a stimulant and alterative influence."^{16(p602)} Koumiss, or conjugated milk products and beef tea, were commonly given to neurasthenics. "Oils and fats like cream and butter," according to Beard, "were nerve food."^{1(p156)} Foods were often combined with stimulants and tonics in an endless assortment of prescriptions for neurasthenia. One passage from the pen of T. W. Fisher reflected: "...rest, strong beef tea at regular intervals, with

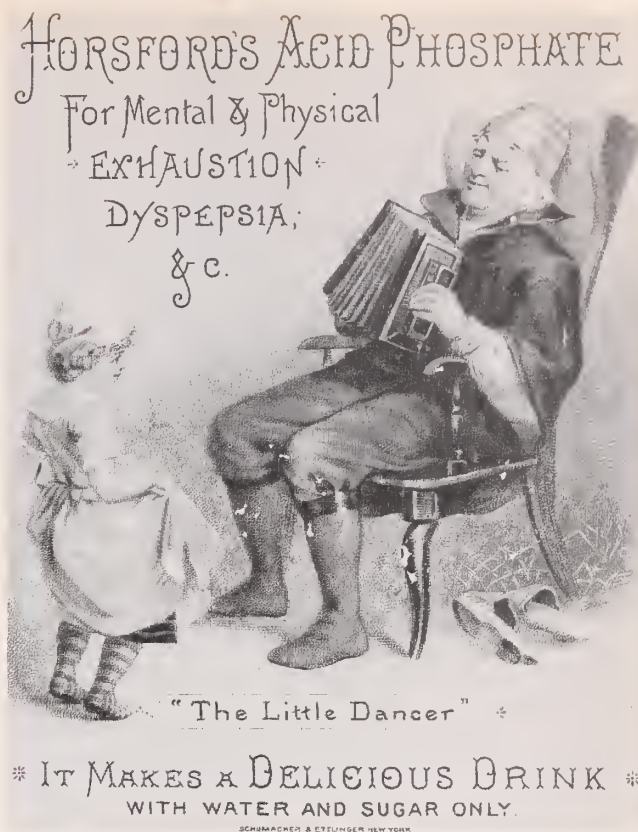


FIGURE 3. A common commercial medicine used for neurasthenia (private collection of John Stea).

capsicum instead of alcohol, seemed first indicated."^{22(p65)} Capsicum, or cayenne pepper, was extracted from the plant *Capsicum annuum* and was used as a stimulant.

COMMERCIAL MEDICATIONS FOR NEURASTHENIA

After the Civil War, medical journals were replete with an ever growing number and variety of commercial medicines, and by the 1870s, many were advertised for the treatment of neurasthenia. They ranged from the crude drugs to mixtures of various substances. "Phosphorus as a remedy" headed a full page promotion in one medical journal in 1883, proclaiming the usefulness of a pill that contained "...unoxidized phosphorus, strychnine and reduced iron" for the "...loss of nerve power, neuralgia and hysteria." In addition to its purported benefit for other conditions, including those of the "cerebro-spinal system as induced by overwork and influences incidental of modern life," the announcement added a regimen to complement "this nerve tonic," including "complete rest of mind, any new hobby or study" and a "very nourishing diet, especially of shellfish."²³ The manufacturer of this pill claimed that another product, Warner's Effervescent Caffeine and Bromide of Potassium, was useful for "sleeplessness, overexertion of the brain, overstudy and nervous debility." While revealing its content of one grain of caffeine to 20 grains of bromide, the ad provided in fine print "...it is not a secret remedy and such as the doctors can use with confidence."²⁴ Another phosphorus preparation, Horsford's Acid Phosphate, was used by Beard as part of one treatment regimen (Fig 3).^{2(p33)} This product comprised ingredients including magnesium, calcium, and sodium phosphate. In 1887, an advertisement for this product described a liquid prepara-

tion of the phosphates and phosphoric acid for "dyspepsia, mental and physical exhaustion, nervousness and weakened energy." The contemporary reader could have noted that on the same page was a commercial for Crosby's Vitalized Phosphites. The passage assured that the product used "a vital phosphite, not a laboratory or soda water absurdity." The ingredients of this product consisted of "nerve-given principles of the ox brain," amalgamated with the embryo of the wheat and oat and would benefit "sleeplessness, irritation, nervous exhaustion and inability to work or study."²⁵ Fellow's Syrup of Hypophosphites, containing "hypophosphites of iron, quinine and strychnine," was advertised in 1902 for the treatment of neurasthenia and also ascribed as effective for the treatment of "anemia, bronchitis and influenza."²⁶ Several products that manufacturers claimed to be advantageous in the treatment of neurasthenia, illustrated a belief in strengthening the blood among 19th century physicians. Maltine, described as an extract of malted barley, wheat and oats, was purported to contain "nitrogenous constituents," with "a composition identical to the chief constituents of blood," in one 1879 advertisement. The ad provided a detailed explanation of its manufacture, adding that Maltine, when combined with iron, quinine, strychnine and phosphorus, was a "powerful nutritive, general and nervous tonic."²⁷ One blood-supporting compound was Crinon's Haemoglobin, described in one 1879 advertisement as the "Albuminoid Ferruginous Principal of Blood," useful in cases of "anaemia cachexias, and exhaustion caused by excess of work and nervous debility. . . ." ^{27(p15)} Dr Buckland's Oats Scotch Essence, a product that actually contained oats, appeared in one medical journal as a "nerve and brain food tonic," yielding "remarkable results for nervous dyspepsia, sleeplessness, opium habit and neurasthenia." It was also described as being in "no sense a patent medicine."^{24(p21)}

Other medicines for neurasthenia that were advertised in the medical journals included the "restorative wine of coca," that was promoted in 1887 as a cure for "nervous prostration, brain exhaustion and all forms of mental and physical debility." The advertisement claimed that the neurologist, William A. Hammond, had endorsed the product at the New York Neurological Society. He is quoted as stating in one meeting:

I therefore asked a well-known gentleman of this city if he would not prepare a good wine and pure alkaloid. He has succeeded on making such a preparation. . . . A wine glass of this tonic taken when one is exhausted and worn out acts as a most excellent restorative. . . . The cocaine appears to have the power to reduce the irritations of the stomach and make it more receptive for food.^{24(p24)}

Another testimonial by Hammond appeared in one advertisement for Buffalo Lithia Water, a solution purported to contain "well defined traces of lithia. I also often prescribe it in those cases of Cerebral Hyperaemia, resulting from over-mental work in which the condition called nervous dyspepsia results."^{24(p6)} It should be noted that subsequent analysis of most lithia waters of the period, revealed only trace quantities of lithium.

PATENT MEDICINES FOR NEURASTHENIA

Many medicines that were available for direct sale to the public, commonly called patent medicines, carried claims for the cure of neurasthenia and nervous debility. Patent

medicine was actually a misnomer, for these products were usually registered under a trademark rather than a patent. The trademark made it possible for the manufacturing process and contents to be maintained in secret. Since many of the more standard medical preparations were also available directly to the public, they too were often termed patent medicines. Popular patent medicines that rarely appeared in the medical journals but were widely consumed included Ayers' Sarsaparilla and Lydia Pinkham's Vegetable compound. Derived from the plant *Smilax officinatus*, Sarsaparilla was regarded for many decades as a panacea, and a tonic. The 1870 *Dispensatory* stated that the herb had been reported to support the body in disease states, including syphilis, rheumatic disease, and mercury poisoning.^{16(p782)} Dr Ayers, of Lynn, Massachusetts, boasted in one advertisement, complete with a picture of a forceful lion, that this product would cure "Thin blood, Anemia, Poverty of the blood, Weakness, General Debility, Nervousness, Nerve Exhaustion, Nervous Prostration, Nervous Dyspepsia, Indigestion, Dyspepsia, Skin Diseases, etc. . . ."²⁸ Another native of Lynn, Massachusetts, Lydia Pinkham, developed a very popular patent medicine in 1876. Her vegetable compound contained the ubiquitous alcohol and herbs, including black cohosh. Derived from the plant *Anucifuga rarenosa*, black cohosh was used as a stimulant and a cathartic. Designed for the "worst form of female complaints," the panacea, also promised to cure nervous prostration (Fig 4).²⁸

Some preparations for neurasthenia, such as Cherry Malt Phosphites, were presented directly to the public as well as to the medical profession. "A combination of wild cherry, the condensed extract of the important cereals and the elixirs of the hypophosphites of lime and soda," the malt drink occupied an entire page in an 1887 edition of *The Boston Medical and Surgical Journal*.^{24(p10)} An advertisement for the same product appeared on a card that same year for distribution to the public. The card depicted a young girl with a dog; the text on the reverse side boasted that the medicine "acts on the stomach and the liver. . . building up the weak and broken down system" and was applicable for the "loss of appetite, headache, insomnia, general debility, malaria and nervous prostration."³⁰

Public consumption of the various over-the-counter medicines that were purported to benefit sufferers from neurasthenia and other illnesses, was catalyzed by the availability of almanacs, books and other literature issued by their producers that described their attributes and by advertisements in catalogues and popular journals. In the drug section of one department store catalogue, there were references to 14 patent medicines that claimed to ameliorate nerve weakness, prostration, or debility. Included were Dr Worden's Female Pills for Women, Brown's Vegetable Cure for Female Weakness, and Celery Malt Compound.³¹ R. V. Pierce of Buffalo, New York, founder of the Invalid's Hotel and patent medicine manufacturer, wrote descriptions in his popular *Common Sense Medical Advisor* (Fig 5). One apparently satisfied customer who had suffered from nervous prostration stated in a testimonial included in the book, "I am getting along so well with the medicine that I am a standing wonder to my friends, and I shall not cease while life lasts to praise the skill that has brought such miraculous results."³² The popular book *Household Physician* devoted an entire section to the patent medicines, the writers of the guide asserting that there were some good patent medicines, including Mellin's Food "for those suffer-

LYDIA E. PINKHAM'S VEGETABLE COMPOUND

IS A POSITIVE CURE.

For all those painful Complaints and Weaknesses
so common to our best female population.

It will cure entirely the worst form of Female Complaints, all Ovarian troubles, Inflammation and Ulceration, Falling and Displacements, and the consequent Spinal Weakness, and is particularly adapted to the Change of Life.

It will dissolve and expel tumors from the uterus in an early stage of development. The tendency to cancerous humors there is checked very speedily by its use.

It removes faintness, flatulency, destroys all craving for stimulants, and relieves weakness of the stomach. It cures Bloating, Headaches, Nervous Prostration, General Debility, Sleeplessness, Depression and Indigestion.

That feeling of bearing down, causing pain, weight and backache, is always permanently cured by its use.

It will at all times and under all circumstances act in harmony with the laws that govern the female system.

For the cure of Kidney Complaints of either sex this Compound is unsurpassed.

LYDIA E. PINKHAM'S VEGETABLE COMPOUND is prepared at 233 and 235 Western Avenue, Lynn, Mass. Price \$1. Six bottles for \$5. Sent by mail in the form of pills, also in the form of lozenges, on receipt of price, \$1 per box for either. Mrs. Pinkham freely answers all letters of inquiry. Send for pamphlet. Address as above.

No family should be without LYDIA E. PINKHAM'S LIVER PILLS. They cure constipation, biliousness, and torpidity of the liver. 25c. per box. — FOR SALE BY

C. F. HAYES,

Prattsburgh, N. Y.



FIGURE 5. R. V. Pierce, New York physician, and patent medicine manufacturer (*The Peoples' Common Sense Medical Advisor in Plain English or Medicine Simplified*, Buffalo, NY, World's Dispensatory Printing Office and Bindery, 1883).

Pointing out the vulnerability to narcotics of individuals who suffered from nervous prostration, Beard wrote in 1880, "when the nervous system loses through any cause much of its nervous force, so that it cannot stand upright with ease and comfort, it leans on the nearest and most convenient artificial support." Chloroform, opium, or alcohol were among the substances that, according to Beard, "may be reported at first an incident, and finally a habit."^{1(p49)} F. M. Hamlin of Auburn, New York, estimated that the number of opium addicts in the United States stood at 500,000 in 1885 and, while commenting on the increase in narcotics consumption, he stated:

"How can we account for this wide-spread and enormous increase? While it is evident all the causes cannot be known, there are some so apparent as need mention only. First and greatest of all is the great increase of the so-called "nervous affections." The victims of these diseases are not only likely to become addicted to the habit themselves, but they are begetting a class of neurotics who are prone to morbid cravings and excesses of every kind their choice of alcohol, opium, chloral or hashish as a stimulant seemingly almost dependent upon accident.... There is no doubt the introduction of the hypodermic syringe gave a great impetus to the use of morphia and from the curiosity excited by its employment afforded greater opportunities for patients to learn what they are taking and what gave them relief."³⁵

Other concerns emerged over the medications used to treat neurasthenia. Reports of side effects and toxicity increasingly surfaced. William Krauss of Buffalo, New York, commented on toxic doses of medicines for nervous disorders in 1900, including strychnine, and urged that the assignment of maximum dosages be given in their application.³⁶

The net effect of all these concerns, coupled with the growing disquietude with other medications that were addictive, inadequately labeled and sold directly to the public, was to precipitate action by the American Pharmaceutical Association, the AMA and the general public, who demanded regulation. The Food and Drug Adulteration Law was passed in New York and New Jersey, for example, in 1881 and entrusted the states' boards of health with monitoring the quality of medicines. In addition that year, the state of Illinois moved to regulate the sale of poisons, including substances used commonly to treat neurasthenia, specifying morphine, strychnine, chloral hydrate, belladonna, and zinc sulfate.³⁷ While the use of medicines for

FIGURE 4. Buried within the plethora of claims for the cure of "Female Complaints," in the advertisement for the patent medicine, Lydia Pinkham's Vegetable Compound, was relief for "Nervous Prostration" (private collection of John Stea).

ing from nervous prostration," Horsford's Acid Phosphate for dyspepsia, and Metcalf's Cocoa Wine as a "stimulating tonic... preferable for mental trouble."³³

CONCERNS FOR THE USE OF MEDICATION FOR NEURASTHENIA

The demand for relief from the 19th century disorder called neurasthenia, paralleled the increase and availability of remedies for the illness. The relationship between the neurasthenic's quest for relief and his faith in available medicines was recognized by Cecil MacCoy, a Brooklyn, New York, neurologist, when he wrote: "...neurasthenies are peculiarly liable to suggestion, and the physician who fails to avail himself of its use drops one of the most important articles out of his list of remedial agents. The history of quackery is full of lessons as to the efficacy of faith," MacCoy continued, "as the prime agent in healing."³⁴ The use of addictive medications within the expanding realm of substances for the relief of neurasthenia, from the standard preparations to the patent medicines, elicited the concerns of many physicians by the late 1800s.

neurasthenia was modified because of the increased awareness of the potential dangers of the contemporary remedies among the medical community as well as the general public, the mental therapies such as hypnosis and later psychoanalysis and other psychological therapies became important both in its treatment and gradual transformation. Gossling pointed out that medications were the most popular treatment for neurasthenia used by physicians in the late 1870s but by the early 1900s, rest, travel and the mental therapies were more commonly prescribed.^{2(p128)}

CONCLUSIONS

The common denominator of the various descriptions of neurasthenia was the presence of fatigue or lack of nervous force. The advertisements of medicines for neurasthenia also revealed an emphasis on the alleviation of exhaustion. In a society that placed great emphasis on strength, industry, and productivity, these symptoms received priority over other features of the disease such as anxiety, depression, and somatic complaints. Victorian physicians recognized that fatigue arose from a number of medical conditions including malaria and consumption or tuberculosis. In addition, 19th century writers on neurasthenia felt that women were endowed with less nerve force, and that the female reproductive system further taxed the nerves, leading to nervous prostration. In the medical and social atmosphere of Victorian America, the subjective experience of exhaustion and malaise were probably related to conditions that we would now categorize under the headings of depression and possibly, such physiological afflictions as premenstrual syndrome or anemia. The higher prevalence of depression among women, together with the premenstrual syndrome, may account for the frequency with which neurasthenia was diagnosed in the female population. Weakness, the symptom common to these conditions, became the cornerstone of the illness known as neurasthenia by the process of filtration through the societal values and medical beliefs of the 19th century.

Many popular and creative people were diagnosed as having neurasthenia during the Victorian era. They included William James, Jane Addams, and Theodore Roosevelt. In his book *American Nervousness 1903*, Lutz examines neurasthenia in the context of societal changes between the Civil War and the first World War. He writes "by 1903, neurasthenic language and representations of neurasthenia were everywhere." Lutz points out that the disease became a marker of status and respectability. By the turn of the century, it permeated every aspect of society.³⁸ Men and women of distinction who were described as neurasthenic served as role models for people with anxiety, depression, and other psychological conditions, who could identify with their afflicted heroes.

The diagnosis of nervous exhaustion must have proven a dilemma for women in the Victorian Era, whose willingness to accept the condition of weakness imposed by the predominantly male physicians of the period contrasted with their increasing desire to participate in an industrial society. The prevailing attitude among these men was a reflection of the prevalent cultural view that women were the weaker sex. Accordingly most in the medical profession thought women to have weaker nerves. Gossling points out that the causes for neurasthenia most commonly reported for women were genital and reproductive disturbances. Even female physicians such as Margaret Cleaves found women particularly prone to neurasthenia. Many physicians also believed that neurasthenia would be induced in

women by emotional stress such as accidents.^{2(pp55-62)} It was easier, nevertheless, for female as well as male sufferers from neurasthenia to accept an affliction that was attributable to a physical condition rather than to mental illness. Manufacturers of medicines took advantage of this preference and in their advertising promised the abatement of exhaustion. These ads promised relief from derangements that exhausted the nerves of energy, as well as the re-energizing of weakened nerves to strengthen the body. In Victorian society, these remedies served as a staple for those who were labeled or considered themselves, weak and languid, stemming from a condition that was thought to afflict the best and the brightest. Although psychiatrists today employ efficacious medications that are aggressively advertised by drug companies, many individuals continue to self medicate with various street drugs, including cannabis, cocaine, opiates and alcohol, substances used as medicines by 19th century physicians treating neurasthenia. Much of the uneasiness expressed by the latter group of physicians with the medicines that were at their disposal for the treatment of neurasthenia, was related to adverse side effects and addiction. That such concerns are no mere remnant of a benighted past is attested by the misgivings expressed by contemporary physicians regarding the too easy, too frequent, and inappropriate use of such drugs as the benzodiazepines.

Acknowledgments. The authors would like to thank Marvin Lipkowitz, MD, Director of Psychiatry at Maimonides Medical Center for his inspiration in the development of the concept of this paper. In addition, we are grateful to the late Eric T. Carlson, MD, Director of the History of Psychiatry section at Cornell Medical Center for his assistance, and Gorden Mestler, Archivist at State University of New York Health Science Center at Brooklyn Library.

REFERENCES

1. Beard GM: *A Practical Treatise on Nervous Exhaustion (Neurasthenia): Its Symptoms, Nature, Sequences, Treatment*. New York, William Wood and Company, 1880, p49.
2. Gossling FG: *Before Freud, Neurasthenia and the American Medical Community, 1870-1910*. Urbana and Chicago. University of Illinois Press, 1987, pp143-162.
3. Abbey SE, Garfinkel P: Neurasthenia and chronic fatigue syndrome: the role of culture in the making of a diagnosis. *Am J Psychiatry* 1991; 148:1638-1646.
4. Van Deusen EH: Observations on a form of nervous prostration (Neurasthenia), culminating in insanity. *Am J Insan* 1869; 25:445-461.
5. Carlson ET: The nerve weakness of the 19th century. *Int J Psychiatry Med* 1971; 9:50-54.
6. Haller JS: Neurasthenia, medicine profession and urban blahs. *NY State J Med* 1970; 70:2489-2497.
7. Beard GM: *Drugs and Alcohol, Stimulants and Narcotics, Medically, Philosophically and Morally Considered*. New York, G. D. Putnam Co., 1871, p59.
8. Rosenberg CE: The place of George M. Beard in nineteenth century psychiatry. *Bull Hist Med* 1962; 36:245-259.
9. Cowles E: The mechanism of insanity. *Am J Insan* 1891; 47:471-495.
10. Collins J, Phillips C: The etiology of treatment of neurasthenia: an analysis of three hundred and thirty-three cases. *Med Rec* 1899; 55:413-422.
11. Beard GM: *Sexual Neurasthenia, its Hygiene, Causes, Symptoms, and Treatment, with a Chapter on Diet for the Nervous*. New York, E. B. Treat and Co., 1884, pp59-60.
12. Douglas Wood A: The fashionable diseases: women's complaints and their treatment in nineteenth-century America. *J Interdis Hist* 1973; 4:25-52.
13. Haller JS: Neurasthenia: the medical profession and the "New Women" of the late nineteenth century. *NY State J Med* 1971; 71:473-482.
14. Bruce-Chwatt L: Chinchona and its alkaloids: 350 years. *NY State J Med* 1988; 88:318-322.
15. Therapeutics. *JAMA* 1900; 34:607.
16. Wood GB, Franklin B: *United States Dispensatory*. New York, J.B. Lippincott and Co., 1870, p403.
17. Andrews JB: The physiological action and the therapeutic uses of the "acidum phosphoricum dilutum." *Am J Insan* 1869; 26:113-129.
18. Percy SR: What is the comparative physiological and the therapeutic action of free phosphorus and the hypophosphites, *Transactions of the Medical Society of the State of New York*, New York, Medical Society of the State of New York, 1876, pp100-125.

19. Squibb ER: Notes on the administration of phosphorus. *Am J Insan* 1877; 33:585-587.
20. Tobey JL: Psycho-therapeutics. *Am J Insan* 1887; 47:427-436.
21. Greene JS: Neurasthenia: its causes and its home treatment. *Boston Med Surg J* 1883; 109:75-78.
22. Fisher TW: Neurasthenia. *Boston Med Surg J* 1872; 9:65-72.
23. Advertisement. *JAMA* 1883; 1:iii (Advertisement Section).
24. Advertisement. *Boston Med Surg J* 1887; 116:15.
25. Advertisement. *Science* 1887; 9:1.
26. Advertisement. *J Adv Therap* 1902; 20:(Advertisement Section).
27. Advertisement. *Boston Med Surg J* 1879; 100:(Advertisement Section).
28. Estes JW: The pharmacology of nineteenth-century patent medicines. *Pharm Hist* 1988; 30:3-18.
29. Advertisement card, from private collection of J. Stea.
30. Advertisement card, from private collection of J. Stea.
31. Israel FI: Editor, 1897 Sears Roebuck Catalogue. New York, Chelsea House Publishers, 1968, (Medical Advertisement Section).

32. Pierce RV: *The Peoples' Common Sense Medical Advisor in Plain English or Medicine Simplified*. Buffalo, World's Dispensary Printing Office and Bindery, 1883, p900.
33. Buffum EH, Warren I, Thorndike W: *The Household Physician, A Twentieth Century Medica*. Boston, Boston Physicians Publishing Co, 1905, p235.
34. MacCoy C: Some observations on the treatment of neurasthenia at the dispensary clinic. *Brooklyn Med J* 1903; 17:339-401.
35. Hamlin FM: The opium habit. *Transactions of the Medical Society of the State of New York*, New York, 1885, Medical Society of the State of New York, pp134-146.
36. Krauss WC: Toxic dosages in the treatment of some nervous disorders. *Transactions of the Medical Society of the State of New York*, New York, 1900, Medical Society of the State of New York, pp214-217.
37. *Proceedings of the American Pharmaceutical Association*. Philadelphia, Sherman and Co. Printers, 1882, pp381-396.
38. Lutz T: *American Nervousness 1903: An Anecdotal History*. Ithaca and London, Cornell University Press, 1991, pp1-30.

The paradise of quacks

JAMES HARVEY YOUNG, PhD

In a new nation and a new century, opined the *New York Daily Advertiser* in 1800, quackery ran rampant as never before in America.¹ The country veritably "teemed" with "medical mountebanks." Patent medicine vendors in every town "fattened on the weakness and folly of a deluded public." Nor were the impostors all natives of the New World. "Foreigners who see this growing passion for patent physic leave their homes to try a soil where weeds of this kind flourish with liberal luxuriance. To put a stop to this species of imposition," the newspaper noted, "is an object worthy of legislative interference." Such an approach to quelling quackery, however, lay a century in the future.

The issue of the *Daily Advertiser* denouncing the nostrum boom contained only a single patent medicine advertisement, touting Dr Church's Genuine Vegetable Lotion, a skin disease cure-all. Yet, the paper's lament was accurate. In the expanding press, patent medicine promotion abounded. Whereas most nostrums were not patented, Samuel Lee's Bilious Pills, the first drug to receive this distinction, in 1796, were advertised early in the new century as far from their Connecticut place of origin as Savannah and St Louis.²

THE COLONIAL LEGACY

American ingenuity and venturesomeness had not been so evident in the colonial years. An occasional itinerant quack sold health wares with extravagant claims. A New York carpenter vended therapeutic cordials; a Boston grocer, a cough cure; a Charleston goldsmith, an eye-water; a Philadelphia widow who was Benjamin Franklin's mother-in-law, an ointment for the itch.^{2(pp17,18)} However, the American market for nostrums, from the early 18th century to the eve of Revolution, was dominated by imports from the mother country.³ The development of printing had led to a proliferation of newspapers in Britain during the 17th century, their pages soon filled with nostrum advertising.⁴ Advertisements for prominent British brands began to appear shortly after the colonial press was established.³ Major exporters to America had their plants in the center of London, once the location of merchants who earlier had

migrated to New England. They shipped their wares in bottles of distinctive shape to retail marketers all along the Atlantic seaboard. Colonial apothecaries, grocers, printers, booksellers, and hairdressers listed in their ads the names of patent medicines just arrived on the latest ships from London. The market grew rapidly until trade interruptions preceding revolution, then war itself, interfered. Some Americans sought to sustain supply by filling empty bottles. When peace returned, British producers sought to regain their lost customers. In 1784, a merchant published in the *New York Packet* a list of the old familiar brands as available for sale:⁵

Medicines approv'd by royal charter, James, Godfry, Anderson, Court-plaster, With Keyser's, Hooper's, Lockyer's Pills, And Honey Balsam Doctor Hill's; Bateman and Daffy, Jesuits drops, And all the Tinctures of the shops, As Stoughton, Turlington and Greenough, Pure British Oil and Haerlem Ditto.

THE 19TH-CENTURY BOOM

Overseas merchants, however, were destined for disappointment. The British proprietaries had become in effect American generics. In the powerful spirit of cultural nationalism generated by independence Americans wanted made-in-America patent medicines, be they patented or, as most were, of secret composition.^{2(pp31-89)} Common schooling prepared an ever larger part of the population to read nostrum advertising. Prevailing heroic medicine as practiced by orthodox physicians came under increasing criticism, and a wave of do-it-yourself sentiment in health care accompanied the democratic wave associated in politics with Andrew Jackson's name. Even in such a more favorable market, competition among proprietors increased, and they were forced to expand the amount of advertising extolling their wares. The drabness characteristic of colonial promotion began to be replaced by imaginative vigor. Nostrum-makers pioneered the psychology of advertising with such success as to expand sales enormously. By mid-century, a pamphleteer could exclaim that "Yankeedom" was "the Paradise of Quacks."⁶ Promoters sought to catch the reader's eye with pictures. The noted woodcut artist Alexander Anderson designed striking devices for at least eight major proprietary products, including Hercules and the hydra for Swaim's Panacea, a cupid for Genuine Court

Address correspondence to Dr Young, PhD, 272 Heaton Park Dr, Decatur, Georgia 30030-1027.

SWAIN'S PANACEA,



For the cure of Scrofula, or King's Evil, Ulcers, Rheumatism, Syphilitic, Mercurial and Liver Complaints, and most Diseases arising in debilitated constitutions, or from an impure state of the Blood, &c. &c.

This Medicine has acquired a very extended and established celebrity both in hospital and private practice, which its efficacy alone has supported upwards of eight years.

FIGURE 1. William Swain of Philadelphia chose Hercules battling the Hydra as his mode of suggesting his Panacea's therapeutic power. The medicine contained sarsaparilla, oil of wintergreen, and corrosive sublimate, the most rigorous form of medicinal mercury (from the *Philadelphia Democratic Press*, April 28, 1827; collections of the Library of Congress).

Plaister, a lion for Low's Oriental Saponaceous Compound, and the patriotic eagle for Union Cordia (Fig 1).⁷ The eagle flew for other proprietors as well; indeed, patriotism became a dominant theme in nostrum advertising. The Stars and Stripes was much on display.⁸ One firm printed the Constitution, running red-ink pitches for its bitters along the borders.⁹ Presidents to be, like William Henry Harrison, and presidents out of office, like Martin Van Buren, seemed to testify for the efficacy of certain nostrums.¹⁰ Representing the Supreme Court, the great John Marshall was advertised as having endorsed Gray's Invaluable Patent Ointment.¹¹ In due course, 50 members of the Congress would praise Pe-ru-na, the highly alcoholic remedy for catarrh (Fig 2).¹²

Other themes that sparked public interest found their way into patent medicine promotion: the consolation of religion, the mystery of the long ago and far away, the contrasting allure of the very new as represented by science and technology, the ambivalent image of that child of nature, the Native American (Fig 3).^{2(pp165-189)} Not only presidents, but the famous in other endeavors, like stage stars and sports heroes, were called upon to proclaim the merits of pills and potions. Yet, as a newspaper editor explained, testimonials "signed by plain, everyday working people" were "regarded as more valuable than the indorsement of celebrities."¹³ Such assurance that others had been cured bolstered belief in the proprietor's promises. By converting common experiences like weariness, sluggishness, gloominess, nervousness, and spots before the eyes

50 Members of Congress Send Letters of Endorsement To the Inventor of the Great Catarrh Remedy, Pe-ru-na.



FIGURE 2. Pe-ru-na, a high alcohol nostrum made in Cincinnati, at the turn of the century had the highest sales volume among American proprietary medicines (from the *Montgomery Advertiser*, January 17, 1904).

into harbingers of dread diseases, nostrum advertisers sought to frighten readers into believing they were doomed unless salvation be secured only by taking the proprietor's product. Explicit claims were made for the certain cure of the most feared ailments. During the nation's centennial year, the respected *Harper's Weekly* contained ads for sure cures of asthma, cancer, cholera, consumption, diabetes, diphtheria, epilepsy, gout, hay fever, nervous ailments, opium addiction, and rheumatism (Fig 4).¹⁴ The magazine was too genteel to accept advertisements for abortifacients and for medicines to cure venereal disease and restore lost manhood, but these could be found in many religious periodicals and almost any metropolitan daily.

Recent scholarship has been less judgmental in discussing unorthodox medical practitioners of the past, including

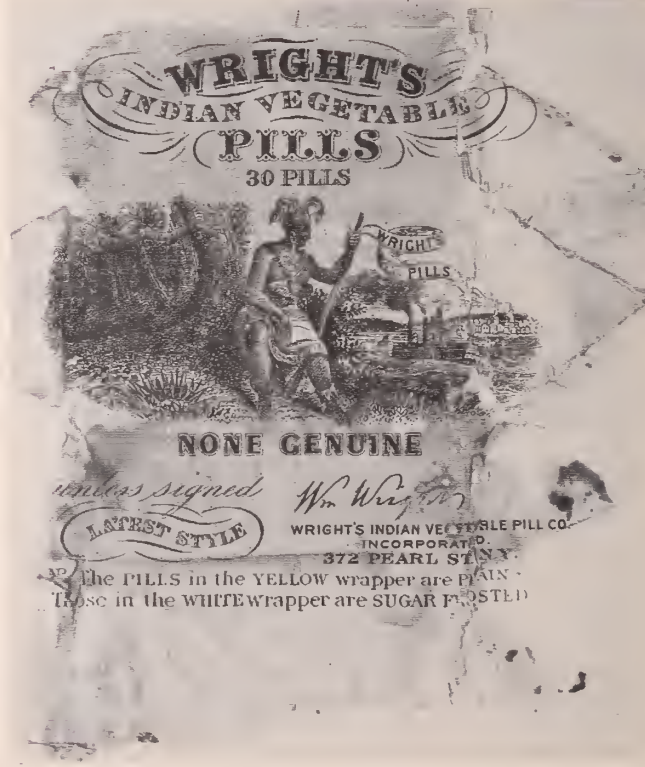


FIGURE 3. Wright's Indian Vegetable Pills featured in the mid-19th century the Native American's purported skill in bringing botanicals from the forest to cure the ills of white city residents (from the author's collection).

FITS EPILEPSY, St. VITUS' DANCE, PARALYSIS, Hysteria, Insanity, and all Nerve, Brain, and Chronic Diseases. A speedy and permanent cure guaranteed. TRIAL FREE. For Circulars, address DR. RUSH, 507 CARROLL AVE., CHICAGO, ILL.

FIGURE 4. In 1876, the genteel *Harper's Weekly*, most popular magazine in the nation, accepted advertising for such dire ailments as epilepsy^{14(p234)} and narcotic addiction^{14(p1063)}.

quacks, than earlier had been the case.¹⁵ J. Worth Estes has demonstrated that the ingredients of many 19th-century patent medicines were the same as those in regular use by orthodox physicians and that therapeutic theories inherent in much nostrum labeling and advertising were in accord with prevailing concepts of professional medicine.¹⁶ Nevertheless, blatant quackery did run rampant.

To define quackery in an earlier age, therefore, looking backward from present perspectives to a time in which medical efficacy rested on less developed scientific foundations, motive must be taken into account. Making categorical claims to cure diseases then recognized by responsible medicine as incurable can be denominated quackery. Making any therapeutic claims for sugar pills or pure pine oil or any other inert ingredient or mixture can also be considered health fraud. The boozers and bracers, their high proof unlabeled and their remedial promises false, must be condemned. So must narcotic soothing syrups for the travails of teething that brought babies to addiction and sometimes to death.

Even some of the patent medicines depending on the use of orthodox ingredients might warrant rebuke. So thought a committee of the Medical Society of the City of New York in 1827 after studying three prominent nostrums, Chambers' Remedy for Intemperance, Leroy's Medicine Curative, and Swaim's Panacea.¹⁷ While discovering that all three contained ingredients useful in therapy, the physicians nevertheless condemned them. "If the untaught empiric be permitted to seize upon the approved remedies of the art," the committee concluded, "and, in order to speculate on suffering credulity, veil them under the specious garb of secrecy, their partial success will confer upon their order, an importance and character that could not be otherwise attained, to the serious detriment of the healing art."

Most military, social, and economic developments during the second half of the 19th century accelerated the boom in patent medicines.^{2(pp93-110,140,141)} During the Civil War, proprietors dumped their remedies wholesale on the Union armies, and the troops took the medicine habit home to their families. The war brought the burden of a tax on proprietaries, but the private die tax stamps that the companies were permitted to design became an effective form of promotion. Fighting the tax brought proprietors together in a trade association that developed potent lobbying skills in state legislatures and the national Congress. Patent medicine makers had pioneered national marketing, and postwar expansion of national transportation and communication networks enhanced this advantage. Advertising became more sophisticated in message, design, and placement. Woodcuts were replaced by lithographs, then lithographs by photoengraving (Fig 5). Nostrum almanacs, in a dozen appropriate languages, entered almost every home in the land. One proprietor boasted that his almanacs were second only to the Bible in circulation. In prewar days a pill promoter, Benjamin Brandreth, reached

FIGURE 5. The Rochester proprietors of Duffy's Pure Malt Whiskey collected for a small fee testimonials from centenarians in the nation's old folks homes attributing their long life to taking Duffy's nostrum (courtesy of the History Office, FDA).

\$100,000 in his annual advertising outlay. Toward the end of the century, the proprietors of Scott's Emulsion and Lydia E. Pinkham's Vegetable Compound each spent \$1 million a year. As the 20th century began, proprietary medicines stood at the head of the list of product categories in money spent each year for magazine advertising (Fig 6).

RIISING CRITICISM AND INITIAL LEGAL RESTRAINT

On the debit side, from the proprietors' perspective, was an increasing criticism of their products. As the sciences developed, this censure became more trenchant; however, it was generally limited to the pages of medical and pharmacy journals, seldom reaching the attention of habitual nostrum buyers. The hazards in patent medicines, however, did concern some state legislators who, beginning in the 1880s, began to propose formula disclosure bills and to include anti-nostrum provisions in food and drug bills.^{2(pp228,229)} The Proprietary Association, aided by newspaper publishers who feared loss of advertising, defeated most such measures. In addition, for many years this alliance kept proprietary remedies out of the definition of drugs in a series of national food and drugs bills that had been before the Congress since 1879.

Such a law did not come until 1906, and public concern about nostrums was a significant factor in moving Congress to act.^{2(pp205-244)} In 1904, a Senate bill defined drugs broadly enough to encompass patent medicines. The year before, Harvey Washington Wiley, chief of the Bureau of Chemistry of the Department of Agriculture and generalissimo of



Painting of the Statue of Liberty in the Harbor of New York.
Presented to M. Mariani by Bartholdi.

"Vin Mariani" seems to brighten and increase all our faculties; this precious wine will give me the strength to carry out certain other projects already formed, for which accept thanks from yours cordially.
Bartholdi.
Commandeur L'igion d'honneur.

FIGURE 6. In an advertising book for the American market, the designer and builder of the Statue of Liberty praised a wine and coca nostrum made in France. Facing title page of *Collective Testimony of the Benefit and Virtue of the Famous French Tonic Vin Mariana* (New York, Mariana & Co, 1910; collections of the Library of Congress).

forces fighting for a law, had first spoken out strongly against the nostrum evil. In 1905, Samuel Hopkins Adams began publication of a series of articles in *Collier's* characterizing patent medicines as "The Great American Fraud." Born in Dunkirk, New York, the son of a minister, Adams had gone to Hamilton College and had then honed his journalistic style by crime reporting on the *New York Sun*.¹⁸ He brought both moral indignation and a respect for hard facts to the nascent muckraking movement that sought to expose the misdeeds of American business and politics.

"Gullible America," Adams began his first article, "will spend this year some seventy-five millions of dollars in the purchase of patent medicines. In consideration of this sum it will swallow huge quantities of alcohol, an appalling amount of opiates and narcotics, a wide assortment of varied drugs ranging from powerful and dangerous heart depressants to insidious liver stimulants, and far in excess of all other ingredients, undiluted fraud. For fraud, exploited by the skillfulest of advertising bunco men, is the basis of the trade."¹⁹

Through his series, Adams buttressed his opening generalization with explicit details, trade name by trade name, about nostrums preying on public fear during epidemics, boozers and bracers converting unwary users into alcoholics, alleged germ-killers containing 99% water, cocaine catarrh powders leading to addiction, pain-killers conducive to heart trouble, and purported sure-cures for incurable diseases. At all levels of the patent medicine business, Adams concluded, "relentless greed sets the trap, and death is partner in the enterprise."^{19(p20)} Patent medicines figured prominently in the final debates before the 1906 law was passed, and that measure paid them significant attention.²⁰ The presence and amounts of certain dangerous drugs—alcohol, opiates, cocaine, chloral hydrate, acetanilide, and several others—must be given on the container's label. All other information provided must be accurate, for the law banned "any statement, design, or device" regarding the medicine or its ingredients that was "false or misleading in any particular." The 1906 law did not aim at curtailing self-medication with proprietary remedies but sought to make the practice safer.

The mere existence of the law brought some self-reform among proprietors, especially a reduction of opiates and alcohol in medications and greater restraint in labeling promises,²¹ but the net gain seemed small. "So far as I have gone," Adams wrote Wiley in 1907, "I find a general disposition to obey the law in the letter, though to evade it as far as possible in the spirit." "Our experience," Wiley replied, "is in accord with yours."²² Wiley, in charge of initiating enforcement actions, gave food his highest priority but launched attacks on the most flagrant abuses respecting self-dosage medications. Campaigns began against headache cures, germicides, treatments for narcotic addiction, broad-gauge tonics, male-weakness remedies, and cancer cures. However, then regulatory initiative hit the stone wall of the Supreme Court.

An eclectic physician named Johnson in Kansas City replied to the charge that his "Mild Combination Treatment for Cancer" was misbranded by denying that the law's taboo on false and misleading promises in labeling applied to therapeutic promises. When the appeals had run their course, the Supreme Court agreed. Congress was not likely to legislate, Justice Oliver Wendell Holmes surmised, in the debatable realm of what could cure and what could not.²³ President William Howard Taft, pointing out that the high court's decision would force the withdrawal of 150 cases pending in the courts, asked Congress to plug the hole.²⁴ The amendment enacted declared a medication misbranded if the package bore a statement or design "regarding the curative or therapeutic effect of such article . . . which is false and fraudulent."²⁵ Quackery did not exist unless the promoter's motive could be proven impure. Although many cases were brought by the Bureau and by its successor, the Food and Drug Administration, during the next quarter century and most of them were won, the burden of proving fraud considerably hampered the control of quackery. So too did omissions in the 1906 law. The misbranding provisions applied only to labeling; advertising was in no way restrained. So a general migration of therapeutic claims took place from nostrum packages to the pages of newspapers and magazines. The law, moreover, applied to foods and drugs but not to devices. The long parade of gadgetry with alleged healing powers that had marched through earlier American history now expanded,²⁶ even though postal fraud actions offered some

restraint.^{21(pp66–87)} Shortly a San Francisco physician, Albert Abrams, profiting from public fascination with the wonders of radio, would develop devices that, he proclaimed, could both diagnose and cure dire diseases over vast distances.²⁷

WAXING AND WANING OF REGULATION

In 1938, the Food, Drug, and Cosmetic (FDC) Act replaced the 1906 law, a New Deal measure coming at the end of a five-year struggle in Congress during which industrial lobbying had been intense.²⁸ While the Food and Drug Administration (FDA) had lost a bureaucratic contest with the Federal Trade Commission as to which agency should police nostrum advertising, a second new law increased the latter's authority.²⁹ In other ways, the new FDC act gave the FDA greater powers of control over quackery. The law introduced control over medical devices. The fraud joker was eliminated: medical science had developed to the extent that the motive of a drug marketer who used false or misleading labeling no longer mattered. Those who transgressed from ignorance as well as those from malice were guilty under the law, both equally deemed a menace to the public health. False labeling was expanded to include not only erroneous positive statements, but also the failure to reveal germane facts, especially the omission of needed warnings. Drugs dangerous to health when used according to directions were outlawed. Drugs and devices that aimed at affecting the body's structure were covered, like those aimed at weight reduction. For non-official drugs, labels must state the common names of all active ingredients, and for a list of potent drugs and habit-forming substances, quantity had to be given. Purported antiseptics must be truly germicidal. New drugs could not be marketed until their sponsors had persuaded Food and Drug officials that the drugs were safe for use under the directions on the label.

During the 1940s and 1950s, the Food and Drug Administration used its new powers to suppress the most hazardous deceptions.^{21(pp191–289,333–389)} A dried thyroid reducing remedy was removed from the market. So were dangerous pain-killers containing cinchophen, aminopyrine, and bromides. Corrosive abortifacient pastes were attacked. A host of dangerous devices were taken to court: nipple shields, bust developers, pile pipes, a battery-powered cure-all named the Electreat Mechanical Heart, and several descendants of Abrams's cure-over-distance gadgetry. An upsurge of nutritional scams, several of them large door-to-door operations, forced FDA to launch actions aimed at restraining excessive claims. The agency closed a dubious diabetes clinic that took patients off insulin and dosed them instead with vinegar and saltpeter. In addition, FDA waged a ten-year campaign to stop Harry Hoxsey from using ineffective medications to treat cancer at his clinic in Dallas (Fig 7).

After all of FDA's efforts at wielding its new weapons, however, the gains seemed so small. Commissioner George Larrick, commenting in 1955 on the agency's "unfinished business," asserted that amazingly the "good old days" of quackery continued "to a very great extent."³⁰ A journalist put the annual cost to the American public at a billion dollars.³¹ The belligerence with which major promoters fought back against regulators seemed astounding. Leaders of unorthodoxy also leagued together for purposes of propaganda and lobbying, and their efforts seemed to be influencing public opinion.

The dangers of burgeoning health fraud struck quackery's foes in the regulatory and medical communities as so



FIGURE 7. The FDA exposed the inability of a horsetail weed nostrum to cure diabetes during the agency's campaign in the 1930s to gain public support for stronger food and drug legislation (courtesy of the History Office, FDA).

threatening that intensified efforts to combat them seemed indispensable.^{21(pp402–422)} The American Medical Association and the Food and Drug Administration combined to sponsor in 1961 a National Congress on Medical Quackery to focus the bright spotlight of publicity on the methods and hazards of pseudoscience in health.³² Three more such congresses followed before the decade ended. Journalists spread the message in the popular media, often doing their own investigations of quack enterprises. Simultaneously the FDA, the FTC, and the Post Office mail fraud division intensified their efforts to enforce the laws against health fraud, placing special emphasis on nutrition nonsense and device deception. The FDA secured a new weapon with the enactment in 1962 of the Kefauver-Harris Amendments, which required proof of efficacy before a new drug could be marketed.³³ Under this law, the agency was able to halt interstate distribution of the falsely claimed cancer "cure," Krebiozen. Many other victories were won by the regulators, but whether the tide of battle had swung their way seemed doubtful. At the third congress on quackery in 1966, a medicolegal prosecutor from California estimated the "overall annual quackery take" in the nation at "two or more billion."³⁴

The reasons for the continuing creep upward in health fraud were many and complex.³⁵ One was the vigor with which the champions of unorthodox therapies fought back. They organized countercongresses and health fairs to publicize their alternative approaches. While condemning their opponents for conspiracy, they brought their own separate segments into tighter liaison, energizing their faithful customers for protest demonstrations and letter-writing campaigns to regulatory agencies and legislative bodies. They centered their propaganda on cherished themes like "liberty" and "freedom." In addition, they increased the subtlety of their promotion, being more careful with their labeling and advertising while placing claims for their products in first-amendment protected magazine articles and paperback books as well as in radio and television programs.

Elements in the broader cultural climate helped quackery to flourish. The 1960s witnessed a rebellion against traditional authorities. Vietnam and Watergate left a legacy of disillusionment with big government, including its regulatory role. Environmental alarms, especially regarding nuclear power, bred skepticism of big science, not least government's scientific function. Novelist Kurt Vonnegut, in time, gave this perspective ironic expression in a commencement address: "We would be a lot safer if Government would take its money out of science and put it in

astrology and reading palms."³⁶ Astrology, indeed, was soaring, making millions for publishers. Palmistry, numerology, and tarot cards gained great popularity. Paperbacks on these themes were among the fastest selling items in university bookstores from Cambridge to Berkeley.³⁷ "Witches," a magazine reported, "are surfacing everywhere."³⁸ Such an atmosphere did not foster a rational approach toward health. "Magic in medicine is back," observed Lewis Thomas, "and in full force."³⁹

The new climate deepened the abiding reservoir of susceptibility to quackery resting on such factors as ignorance, gullibility, the placebo effect, a suspicion of elites, the miss-no-bets attitude, and panic when confronted with the diagnosis of a dread disease.⁴⁰ No physician should be surprised, William Osler once remarked, if he should "discover accidentally a case of Warner's Safe Cure in the bedroom of. . . [his] best patient."⁴¹

One other crucial factor aided the expansion of unorthodoxy in the 1970s. The antiquackery crusade of the previous decade declined from its high plateau of intensity.⁴² The American Medical Association, dominant in the campaign of nostrum fighting since early in the century, while not abandoning the role entirely, in 1975 abolished its quackery committee and its Department of Investigation. Liaison among regulatory agencies and voluntary health associations languished. Their major joint educational campaign against quackery lapsed. Federal regulators, with many duties to perform and tight budgets, gave combating quackery a lower priority, especially schemes that cheated but did not pose threats to health. Food and Drug Commissioner Arthur Hull Hayes, Jr. commented in retrospect that the agency had been "simply over-matched. . . . There are too many quacks, too skilled at the quick change of address and product name, for the cumbersome procedures of FDA."⁴³ Congressman Claude Pepper agreed that the regulatory agencies had not been doing a satisfactory job. The recent boom in quackery, he concluded in 1984, had resulted from its "immense profitability and apparent absence of risk."⁴⁴

Congress itself shared the blame. Pressed by the mounting mail stimulated by the leaders of nutritional unorthodoxy, Congress in 1976 enacted a law sharply reducing the FDA's authority to control over-the-counter nutritional products.^{45,46} The media also played a heavy role. The interpretation of unorthodoxy in print and over the airwaves largely lost the skepticism of the sixties and presented instead a favorable view. Especially was this true of the checkout-counter tabloid press, in which science, David Leff observed, amounted to a "neo-medieval fantasy world of magic, mystery and miracle."⁴⁷

RECENT REVIVAL OF CONCERN

At the hearing of Congressman Claude Pepper's subcommittee in 1984, Victor Herbert, then a professor at the New York Downstate Medical Center and now at the Mount Sinai School of Medicine, gave his educated estimate of the nation's annual quackery financial toll.^{44(pp88-91)} He put the figure at \$25 to \$26 billion, a more than 12-fold increase since John Miner's estimate in 1966. Herbert sought to categorize the types of quackery on which the largest sums were squandered. Six billion dollars went for "food supplement, pill, powder and potion quackery," and about \$3 billion each for arthritis, cancer, and heart disease quackery.

The Pepper subcommittee's inquiry with the attendant publicity was one force reawakening concern about quack-

ery's growing presence. Another factor was the persisting battle over Laetrile, the specious cancer drug, being fought in state legislatures, federal courts, regulatory agencies, and the realm of public opinion.^{46(pp205-255)} Never before had a single unorthodox health substance developed such powerfully organized and well-financed pressure groups to contest for its acceptance, seeking to override the legal procedure for admitting new drugs. Still a third crucial event was the arrival of acquired immunodeficiency syndrome, a fearsome incurable disease, spawning a plethora of fake cures and preventives, "a jungle of truly questionable and quack products," as Commissioner Angelo J. Aponte of the New York Department of Consumer Affairs put it.^{46(pp256-285),48} Anti-quackery forces revived their alliances and resumed the battle. The war was to be fought on many fronts, not least the ideological. The ranks of unorthodoxy were proclaiming a counter-paradigm to that of scientific medicine, two philosophers pointed out, seeking to persuade the public that their logic was sounder, their therapy more effective than those of the medical establishment.⁴⁹ "Too many people seem willing to swallow the rhetoric—even too many medical doctors—and," the philosophers asserted, "the result will not be benign." A recent assessment escalates the nation's annual quackery imposition to \$40 billion.⁵⁰ America may still be deemed a paradise of quacks.

REFERENCES

1. *New York Daily Advertiser*, September 18, 1800, citing *Gazette of the United States*.
2. Young JH: *The Toadstool Millionaires*. Princeton, Princeton University Press, 1961.
3. Griffenhagen GB, Young JH: Old English patent medicines in America, in *Contributions from the Museum of History and Technology*, United States National Museum Bulletin 28. Washington, Smithsonian Institution, 1959.
4. Hambridge RA: "Empiricism, or an Infatuation in Favour of Empiricism or Quackery." The socio-economics of eighteenth-century quackery, in *Literature and Science and Medicine*. Los Angeles, William Andrews Clark Memorial Library, 1982.
5. *New York Packet and the American Advertiser*. October 11, 1784.
6. *Humbug: A Look at Some Popular Impositions*. New York, S. F. French, 1859.
7. Alexander Anderson proof book. New York Public Library.
8. Isham's Celebrated Stomach Bitters label. Prints and Photographs Division, Library of Congress.
9. Pendleton's Calisaya Tonic Bitters pamphlet. Map and Print Division, The New-York Historical Society.
10. Tippecanoe Bitters poster. Warshaw Collection, Archives Center, National Museum of American History, Smithsonian Institution; Whitcomb's Asthma Remedy ad. *NY Times*, May 5, 1866.
11. *New York Transcript*, November 2, 1835.
12. *Montgomery Advertiser*, January 17, 1904.
13. *New-Orleans Times-Democrat* cited in *Drug Circ and Chem Gaz* January 1901; 45:xi.
14. Young JH: *Harper's Weekly* on health in America, 1876. *J Hist Med Allied Sci* 1986; 41:169-171.
15. Wear A: Introduction, in Wear A (ed): *Medicine in Society: Historical Essays*. Cambridge, Cambridge University Press, 1992.
16. Estes JW: The pharmacology of nineteenth-century patent medicines. *Pharm Hist* 1988; 30(1):3-18.
17. Reports of the Medical Society of the City of New-York, on Nostrums, or Secret Medicines, New York, The Society, 1827.
18. *NY Times*, November 17, 1958.
19. *Collier's*, October 7, 1905; January 13, 1906.
20. Food and Drugs Act, June 30, 1906, 34 US Stat 768.
21. Young JH: *The Medical Messiahs*. Princeton, Princeton University Press, 1967.
22. Adams to Wiley, March 26, 1907; Wiley to Adams, April 1, 1907. Bureau of Chemistry General Correspondence, Record Group 97, National Archives.
23. *United States v Johnson*, 221 US 488, May 29, 1911.
24. *Congressional Record*. 62d Congress, 1st sess, pp2,379-2,380.
25. Sherley Amendment, August 23, 1912. 37 US Stat 416.
26. Young JH: Device quackery in America. *Bull Hist Med* 1965; 33:154-162.
27. Pollack CV: Electronic therapeutics of Albert Abrams, MD. *Pharm Hist* 1984; 26:109-113.
28. Jackson CO: *Food and Drug Legislation in the New Deal*. Princeton, Princeton University Press, 1970.
29. Wheeler-Lea Act. 52 US Stat 111.
30. Larrick GP: Our unfinished business. *Food Drug Cosm Law J* 1955; 10:168.

31. Cook J: *NY Post*, May 20, 1957.
32. Proceedings, National Congress on Medical Quackery. Chicago, American Medical Association, 1962.
33. 76 US Stat 780.
34. Miner JW: The costs of quackery. Mimeographed text of October 8, 1966 address.
35. Young JH: The foolmaster who fooled them. *Yale J Biol Med* 1980; 53: 555-566.
36. Wolcott J: Mod apostle. *NY Rev Bks*, November 22, 1979.
37. Kremen B, Collier P: Unrequired Reading: East and West. *NY Times Bk Rev*, February 15, 1970, part II.
38. Vachon B: Witches are rising. *Look*, August 24, 1971; 35:40-44.
39. Thomas L: *Medusa and the Snail*. New York, Viking, 1979.
40. Young JH: The persistence of medical quackery in America. *Am Scientist* 1972; 60:318-326.
41. Osler W: *Aequanimitas* Philadelphia, Blakiston, 1932.
42. Young JH: Afterword, in Young JH: *The Medical Messiahs*, expanded ed. Princeton, Princeton University Press, 1992.
43. Quackery: A \$10 Billion Scandal. A Report by the Chairman of the Subcommittee on Health and Long-Term Care of the Select Committee on Aging. House of Representatives, 98th Congress, 2d session, 1984.
44. Quackery: A \$10 Billion Scandal. Hearing before the Subcommittee on Health and Long-Term Care of the Select Committee on Aging. House of Representatives, 98th Congress, 2d session, 1984.
45. Health Resources and Health Services Amendments, 90 US Stat 401.
46. Young JH: *American Health Quackery: Collected Essays*. Princeton, Princeton University Press, 1992.
47. Leff D: Four wondrous weeks of science and medicine in the amazing, incredible supermarket press. *Nat Assn Sci Writers News* 1980; 2(1):3.
48. Aponte AJ: Text of lecture before the National Association of Consumer Agency Administrators convention, June 12, 1987.
49. Glynmour C, Stalker D: Engineers, cranks, physicians, magicians. *N Engl J Med* 1983; 308:960-964.
50. Barnhill W: Panacea or poison? *Arthritis Today*, January-February 1992.

Kindly medicines

A history of the physio-medicals in American medicine

JOHN HALLER, JR, PhD

The school of physio-medicalism originated with the founding of the Botanico-Medical Institute in Columbus, Ohio, in 1939. Seven additional colleges were established before the Civil War; all but two closed before 1862. A scattered few opened in the last quarter of the 19th century and followed a similar fate. The physios, as they were popularly known, were direct descendants of Samuel Thomson's botanic medicine and emerged as a separate school under the leadership of Alva Curtis (1797-1881) in the 1840s. Until its last college closed in 1911, physio-medicalism remained the lone surviving element of reform Thomsonianism in the United States. Its history illuminates both the promises and the delusions of 19th century sectarian medicine.

THOMSONIANISM

Physio-medicalism originated in the observations, experiences, discoveries, and declarations of Samuel Thomson (1769-1843) of Alstead, New Hampshire, who founded a patented system of botanic therapeutics in the 1820s that spread through the northeast, south, and middle-west with a fervor that paralleled the growth and popularity of religious sectarianism in the early 19th century (Fig 1). There was little new in Thomson's medicine bag: the substitution of botanic medicines for mineral drugs, and a therapeutic regime that promised to clean out the intestinal tract and feed the patient tonics that had been popular among the Native Americans. The principles of his system, however, were surprisingly similar to regular medicine in both philosophy and effect. Nevertheless, his followers credited him with starting "one of the grandest reforms that has ever yet claimed the attention of any people."^{1,2} The particular strength of Thomson's popularity lay in his democratic appeal, offering to all who were willing to pay \$20 for rights to his 1813 patent (renewed in 1823 and again in 1837), the opportunity to cure themselves of sickness and

disease without dependence on the pretensions of a learned profession. Here was a calling open to men and women alike, a system of self-help which allowed families to meet their health needs by a patented process of therapeutic measures. In the heyday of Thomson's leadership, the movement opposed the establishment of medical schools, infirmaries, and medical societies—all of which implied the need for a professional medical class. Instead, Thomson (known affectionately as "Old Sammy"), offered a system of health care compatible with the do-it-yourself philosophy of the common man. Although regulars condemned Thomson as an ignorant farmer, his success at marketing his patented system far outpaced his enemies' expectations given his "unlettered" background. The principles which he advocated in his *New Guide to Health* (1825), especially the idea of non-poisonous medication, appealed to a broad spectrum of American society. Indeed, Thomson's patented system offered a non-threatening alternative to the regulars' use of depletive drugs and practices in treating fevers, colics, dysentery, rheumatism, and other illnesses where sweating was deemed efficacious.³⁻⁸

Things were not always as they seemed, however. After a decade or more of Thomson's authoritarian and anti-intellectual leadership, the botanic movement matured to the degree that his followers began establishing infirmaries and advocating formal education as an essential component of the movement's future.⁹ Those followers of Thomson who came from the "more liberal and better educated classes," felt strongly the necessity of medical education to prepare doctors for their profession. These same individuals considered it important to expand Thomson's materia medica to include other remedies, most of which the founder vigorously opposed. This deviation in the practice of herbal medicine resulted in a schism that marked the end of Thomson's personal influence over the movement and the emergence of an era of new leadership.^{3(p237)}

Much of the criticism leveled at Thomson derived from his decision to limit his health care system to those who had bought the rights to his patent. Moreover, he opposed the establishment of medical colleges, insisting that medical

From the Department of History and Medical Humanities, Southern Illinois University at Carbondale, Carbondale, IL.

Address correspondence to Dr Haller, Southern Illinois University at Carbondale, Coyer Hall, Carbondale, IL 62901-66801.



FIGURE 1. Samuel Thomson (courtesy, New York Academy of Medicine).

education had become the private reserve of educational elitists. Instead, Thomson favored the establishment of Friendly Botanical Societies whose avowed purpose was to share information and cures and thereby bridge gaps in individual practice and experience. He thus tied himself to a position that opposed instruction in anatomy, surgery, and other branches of medical science, and his more intellectual and educated followers soon became restless. According to botanic reformer E. Anthony writing in 1886, those who had cast their lot with Thomson and followed his example had foolishly turned against education. Nevertheless, it became "plainly evident that uneducated men could not any longer compete with those who possessed even a meager collegiate education." Given the predicament Thomson had forced on the botanics, and believing that his narrow views had delayed the progress of botanic medicine, those who had admired and supported his cause soon found it necessary to break from his grasp. "Had he wielded the same influence for the organization of colleges, that he did in the establishment of his practice," concluded Anthony, "there might be today a prosperous college in every State in the Union."³(p232-233)

THE PHYSIO-MEDICALS

In contrast with Thomson who explained the purpose and extent of the practitioners education as the "study of patients, not books, experience, not reading," Alva Curtis encouraged a didactic education that more closely paralleled contemporary medical training. Consistent with this approach, he advocated the establishment of colleges and infirmaries in Maryland, Georgia, Mississippi, Tennessee, Ohio, and New York, dedicated to the theory and practice of "sanative" (supportive) medicine. Over a period of two decades, Curtis and this reform wing of Independent Thomsonians transformed the self-help movement of Thomson from a highly charged mass movement representing grass roots democracy, anti-monopoly, and a therapeutic regimen of steam and puke, into a school of medicine that was quasi-intellectual, boasting a half dozen medical colleges that borrowed heavily from the symbols of science and regular medicine.⁹(p426),¹⁰(p337)

Although the physios regarded Thomson as the founder of botanic medicine, they recognized Curtis as the venerable father of physio-medicalism. Born in Columbia, New Hampshire, Alva was the son of Chauncey Curtis, a soldier of the American Revolution. In 1815, he became a teacher of Latin and mathematics on Long Island. After three years, he used his savings to enroll in a two-year program at Union College. When one of his brothers reportedly died

from a mercurial treatment, Alva became attracted to medicine but, lacking money, accepted charge of the female department of Wenton Academy. During that time, he studied medicine under the mentorship of a Dr McKelway and discovered what he believed were well-founded objections to allopathic practice.

In 1820, Curtis enrolled in a course of lectures on botany, followed by a year of traveling around the country, supporting himself by selling book subscriptions. In 1821, he moved to Richmond, Virginia, where he taught language in Mrs Broomes Female Seminary. In 1827, he opened his own seminary and, although the evidence is not clear, he supposedly became enamored with the abolitionist ideas of William Lloyd Garrison. In 1831, he converted to Thomsonianism after seeing its effects on his sister and brother and, during the cholera epidemic of 1832, treated students and himself in accordance with the Thomsonian method. In practicing Thomsonianism, Curtis simply availed himself of a movement already rooted in Virginia through the earlier efforts of William Fonerden, a clergyman and botanic healer. Before long, however, Curtis became the movement's best known figure in Virginia where, having become a general agent, he marketed Thomsonian books, patents, and medicines; organized Friendly Societies; popularized the sect's extraordinary cures; castigated traditional medicine; offered instruction; and managed an infirmary.¹¹(p173)

Curtis' decision to support Garrison and to practice Thomsonian medicine brought opposition from the community, including the medical fraternity; not surprisingly, his actions resulted in a decline in the academy's enrollments. Forced to close the school, Curtis moved to Columbus, Ohio, in 1834 where he devoted himself exclusively to the practice of medicine and gathered around him a number of students and enthusiastic disciples. In 1835, Curtis assumed editorship (replacing Thomas Hersey) of the *Thomsonian Recorder* (1832-1890), the first periodical marketed in the West in the interest of Thomson's botanic medicines. The journal was published by Jarvis Pike and Company and subsidized by Thomson, who utilized it as the sect's official organ. Curtis also opened the unchartered Botanico Medical College and Infirmary in April of 1836 to instruct others in the practice of sanative medicine. Although the school started without a charter—and certainly contrary to Thomson's own bias against the establishment of medical schools—it did not lack students, many of whom followed Curtis from Virginia.⁵(p325),¹¹,¹² Ever an entrepreneur, Curtis encouraged botanic societies to raise a fund for the education of young men who could be sent to the college for training. By selecting those "of the best talents and moral principles, and lend them, without interest, on bond payable when they shall have earned the money (say yearly after they enter practice) so much as they shall need to enable them to prepare themselves well for the work," Curtis thought he had found an alternative source of "thorough-bred Thomsonians" to counter the elitist ranks of allopathic medicine.¹³

In response to inquiries respecting the school, Curtis gave the following information:

On the first of April we commenced the systematic and constant instruction of a Class of young gentlemen, in the true theory and Practice of Medicine. The principles of the science are clearly explained and illustrated, in so great a variety of ways as to fix them permanently in the mind. Our practice affords ample means of exhibiting to students the symptoms of disease, the modus operandi of medicines, and the various and most convenient and proper

ways and means of rendering the remedial agents and the curative processes effectual. The science of Botany is familiarly and practically taught in such a manner as not only to acquaint the student with the botanic *Materia Medica*; but to enable him to examine the whole vegetable kingdom with pleasure and profit. It is illustrated, not merely by books and plates, but by anatomical examinations of the natural subjects, and by oral instructions in the field, as well as in the lecture room. Each student is taught to label and preserve plants for his future benefit. Instructions are given and Lectures delivered on Natural Philosophy and Chemistry. Much attention is devoted to Midwifery, and the forms of disease peculiar to women and children. Anatomy, Physiology and Surgery receive all desirable attention, and the old theories and practices meet their just due, in thorough examination, and comparison with the Botanic.¹⁴

Curtis used a variety of texts in his instruction, including Thomson's *New Guide to Health*, Samuel Robinson's *A Course of Fifteen Lectures*, articles from the *Thomsonian Recorder*, Constantine S. Rafinesque's *Medical Flora*, Benjamin Smith Barton's *Elements of Botany*, Amos Eaton's *Manual of Botany*, and his own books. He offered students use of his library and a room in which lectures and instruction were given. Tuition was a dollar a week, plus an additional three dollars weekly for room and board. The course lasted from six to 18 months, depending on the students background and abilities.^{7,8,15-18}

The first chartered medical school of the Thomsonian schismatics was the Literary and Botanico-Medical Institute of Ohio, founded by Curtis on March 3, 1839, in Columbus, Ohio. Its first class opened with 12 students, and lectures were given three months each year. In 1841, the college moved to Cincinnati, where it changed names regularly (sometimes called the Botanico-Medical Institute, the Botanico-Medical College, or Literary and Scientific Institute) until 1850 when it adopted the name Physio Medical College until closing in 1880. The first home for the college in Cincinnati was Madame Trollope's Bazaar Building (Fig 2). The college later moved to several other

buildings but none had the flair and reputation of the Bazaar, one of the city's more notable historic structures.¹⁹

During its years in Cincinnati, the college became the intellectual center for the Independent Thomsonians, later known as the physio-pathists in the east and the physio-medicals in the mid-west. These appellations did not come without controversy; indeed, the reform wing of the Thomsonians suffered from the effects of regionalism, the lack of an enduring national association, and the fact that botanic reformers seemed less suited by temperament to a single source of authority (Fig 3). As a result, the names "medical reformer," "physio-pathic," and "physio-medical," were used interchangeably in the early years following the schism.^{11(p172)}

NATURAL OR SANATIVE MEDICINE

Physio-medicalism was based on the principles of science, art, and reformation. In science, the physios abandoned all chemical or materialistic theories of life and substituted a physiology based on the concept of vitalism and on the inherent power of the body's vital force. In art, they promoted the physicians power to cure based on the

THE PHYSIO MEDICAL JOURNAL

7

Chicago Physio-Medical College

605 West Van Buren Street, Chicago, Illinois.

SESSION 1892 AND 1893

BOARD OF TRUSTEES.

E. W. LYMAN, President, 161 La Salle Street.
CHARLES LANE, Secretary, 84 La Salle Street.
J. E. ROOP, W. A. HARRIS
H. J. TREAT, F. O. BROADY, H. A. HADLEY

FACULTY

J. E. ROOP, M. D., 1190 W. Harrison Street,
Professor of Obstetrics and Gynecology.
W. F. TAIT, M. D., Galesburg, Ill.,
Professor of Surgical Institutes and Special Diseases.
W. H. COOK, A. M., M. D., Chicago Opera House Building.
Professor of Science of Medicine, Nervous Diseases and *Materia Medica*.
H. P. NELSON, M. D., 605 W. Van Buren Street,
Professor of Practice of Medicine and Clinical Medicine.
H. J. TREAT, M. D., 626 Monroe Street,
Professor of Practice of Surgery, Ophthalmology and Otology.
W. F. TAIT, M. D., Physio-Medical College.
Professor of Minor Surgery and Surgical Anatomy.
S. F. HESKETT, A. M., M. D., 6824 Sherman Street,
Professor of Sanitary Science and Pharmacy.
F. O. BROADY, M. D., 118 Oak Street,
Professor of Histology and Pathology.
W. A. HARRIS, Physio-Medical College.
Professor of Diseases of Children.
W. C. LOAR, M. D., 3631 Cottage Grove Avenue,
Professor of General and Descriptive Anatomy.
W. F. PECHUMAN, M. D., 605 W. Van Buren St.
Professor of Physiology and Microscopy.
H. A. HADLEY, M. D., 1307 W. Van Buren Street,
Professor of Chemistry, Toxicology and Demonstrator of Anatomy.
M. C. KEITH, M. D., Minneapolis, Minn.
Lecturer on Helminthology, Obscure Diseases of the Intestines.
F. W. MITCHELL, M. D., 1221 W. Van Buren St.
Lecturer on Diseases of Nose, Throat and Rectum.
CHARLES LANE, A. B., 84 La Salle Street,
Lecturer on Medical Jurisprudence.

J. E. ROOP, M. D., President.

H. P. NELSON, M. D. Secretary.

The Collegiate year begins on Tuesday, September, 20th 1892, and ends on Wednesday, March 20th, 1893.

FEES—Professors' Ticket, \$65.00; Demonstrators' Ticket (including material), \$10.00; Hospital Ticket, \$5.00; Deposit against breakage in Laboratory (returnable), \$5.00; Matriculation, one term only, \$5.00; Graduating Reviews, \$30.00; Graduates from other schools, \$40.00.

For further information and catalogue, address the Secretary, at 605 West Van Buren Street.

FIGURE 3. Advertisement for a course of study at the Chicago Physio-Medical College, 1893 (from Juettner O¹⁹).

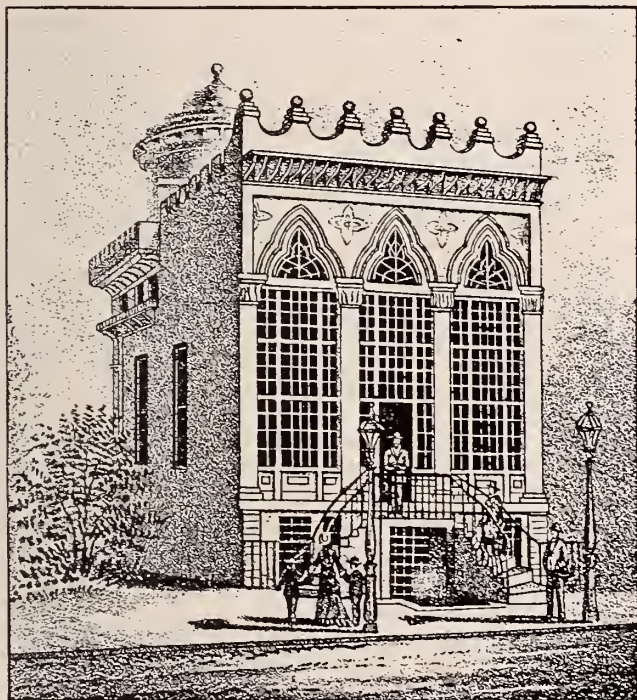


FIGURE 2. The home of the physio-medical college in Cincinnati (from Juettner O¹⁹).

belief that Nature served as parent and guide to the judicious employment of measures that were in harmony with the body's vital force. Thus, the physician had the duty to assist the life power or vital principle by using only those measures. Finally, the physios demanded the same recognition accorded other schools of medicine. This meant the opportunity to work in army and navy hospitals, asylums, and other institutions supported by public taxes; equal privileges with other schools in all medical laws; equal representation on all state medical boards; and exemption from any professional "rulings" that were made in their absence. Throughout their history, the physios made every effort to characterize regular or allopathic medicine as the mirror image of religious orthodoxy and themselves as righteous and patriotic reformers seeking a more volunteeristic approach to health care.²⁰

Since the first great principle of physio-medical practice was the belief in vitalism, the vital force, and not the physician, was the essential healer of disease. Although the physician should sometimes "lead" vital force, he must never "supersede or usurp its legitimate province." This meant working with vital force, not against it; aiding the *vis medicatrix naturae*, or the healing power of nature, not hindering it; using "sanative" therapeutics, not toxic agents; sustaining and guiding vital action, not destroying it; and relying on repletion, not depletion.^{21(p317,324)}

The system of physio-medicalism claimed to be founded strictly on the immutable and infallible laws of nature. This idea, represented in the term "natural medicine," held that physio-medicalism was error free and guided solely by the laws of nature. Fever, inflammation, and irritation were simply manifestations of the vital force attempting to cure disease. As such, they were to be aided rather than opposed by medication. In this regard, the physios accused allopathy of misunderstanding the true nature of these signs, holding, for example, that fever was destructive of the organism rather than representative of the body's recuperative efforts. Accordingly, the physios rejected antipyretic treatment and, not surprisingly, received considerable criticism for their views.²²

In their choice of medicines, the physios were remarkably similar to the early Thomsonians. Lobelia, capsicum, and the vapor-bath remained the sheet-anchors of both systems. True, the physios expanded the materia medica of Thomson, but their list of sanative medicines was well within the contours of Thomsonian practice. Although they were quick to point out the crudities and errors of Thomson, the physios never lost sight of his medical principles.²² "Our remedies are all simple," explained botanist Horton Howard in 1854, "as nature herself is simple." Moreover, physio-medicines were harmless toward nature, but powerful in opposing disease and restoring health. Instead of "preying. . . upon the vital power, and thus contaminating the fluids and destroying the tone of the organs," physio-medical medicines were truly therapeutic in their effect on disease.^{23(p6)} Any therapeutic remedy must first be a true medicine, that is, one whose inherent constituency was "kindly accepted by living matter," thus forming a "harmonious aid" to the vital force which maintained normal physiologic balance.^{21(p245)}

As late as 1903, the physios accused the regulars of using at least 107 poisons in their daily practice. These included 27 combinations of phosphorus, 5 of strychnia, 47 of mercury, 25 of opium, and 14 of arsenic. Regulars responded that a little poison was sometimes a good thing.

The physios retorted that the law of physics had established that the property of matter was constant, that is to say, "what is an inherent characteristic of any substance is continually the same and is impossible to change while the matter itself is unchanged." For that reason, a poison retained its essential nature for all times and was in a condition to kill living matter. "No mans skill," argued F. O. Broady in 1903, "though he be a demi-god in the brilliancy of his powers, can change the tendency of alcohol, arsenic, opium, strychnia, belladonna, aconite. . .to destroy each its own peculiar form of tissue according to its special power."²⁴

HERBAL REMEDIES

Dr Oliver Phelps Brown, author of *The Complete Herbalist; Or, the People Their Own Physicians* (1872), observed that the entire universe consisted of contrary elements (ie, negative and positive principles) which worked in harmony with the laws of nature. Both disease and its cures were embodied in the same positive and negative forces. Brown also held that plants indigenous to a given locality or country were the proper basis of herbal medicines for an individual from that area; plants introduced from other countries were "lessened or deprived of their virtues." The same held true for the "virtues" of a plant growing in a wild or natural condition versus those artificially cultivated. The wild dandelion, for example, possessed rare virtues in affections of the liver, kidneys, and respiratory organs. In its cultivated state, however, it lost its medical attributes. The botanical garden of America is so great that if rightly investigated, argued Fred G. Hoener in 1887, furnishes ample remedies for every curable disorder incident to mankind. He concluded that the creator had planted natural medicines in every field and, to the extent that physios followed nature's direction, could keep patients in a progressive state of health and comfort far better than the allopaths, eclectics, and homeopaths using noxious minerals.²⁶

The materia medica of the physio-medicalist was replete with agents that cured rapidly, effectually, and without benumbing the system. Each drug had its "favorite locality" in the organism and each had its own special mode of action. For example, chills resulted from the liver attempting to remove "effete," "vitiated," or "worn out" materials in the system. "As long as people can be made to believe that they are diseased by a portion of germs or microbes instead of a clogged liver," wrote Melville C. Keith, MD, they could be tricked into swallowing poisons such as calomel, mercury, and arsenic. In place of these harsh metals, Keith recommended the use of verbena and capsicum or leptandra and capsicum prescribed originally by Thomson, Curtis, and William H. Cook, to open up the clogged skin.^{27(pp14,15)}

For Curtis, the treatment of disease required the physician to first relax constricted tissues in order to stimulate secretion and depuration; second, to stimulate the tissues to healthy action; and third, to restore and maintain healthy tone and condition. In achieving this first objective, he prescribed water, warm or cold, in fomentation, tepid, or vapor baths; or cold wet cloths, baths, or affusions, aided by "anti-spasmodic medicines" such as lobelia, eupatorium, catnip, asarum, sage, and soothing aromatics. To achieve the second objective, Curtis used heat, moist or dry, accompanied by capsicum, ginger, xanthoxylon, cloves, and pennyroyal. Finally, to restore healthy tone, he prescribed

gentle, steady, and permanent relaxants and stimulants, good food, pure air, exercise, and cheerful company.^{28(p189)}

For fever, particularly if the patient lived in "hygienic ignorance," the physio-medicalist recommended that the entire perspiratory apparatus be "thoroughly antiseptized." This meant the administration of a steam or vapor bath, followed by "a good old-fashioned hot water and soap scrubbing" to soften the accumulations in the glands, encourage perspiration, and render the skin less susceptible to bacteria. The physician followed this regimen with frequent sponging with boiled soft water to which was added various salines, alkalies, or acids as desired. With this under control, patients were then given caulophyllum and viburnum as ganglionic stimulants; asarum and xanthoxylon frax as capillary stimulants; and cola acuminata or erythroxylon cola for the central nervous system. Curtis also prescribed buchu and juniperus for their properties as active diuretics.^{21(pp97,98,102)}

Phthisis, or consumption, received special notice by the physio-medicalists, who felt they had found a treatment more successful than that employed by regulars and the hordes of patent medicine vendors. In their effort to identify the cause of consumption, the physios concluded that there were many factors which would sooner or later make the system vulnerable to the disease. Any habit or condition that devitalized the system and bankrupted its vital force furnished a fertile soil for consumption. To this end, the physios warned against onanism, excessive venery, spermatorrhea and leucorrheal discharges, nocturnal emissions, long nursing of children, tight-lacing, and poor ventilation. They also condemned belts and recommended suspenders for men and warned women to avoid corsets or elastics to hold up stockings. All clothing should be suspended from a jacket or vest and not from the hips. Then too, patients were to avoid feather beds, sleep only in well-aired apartments, take exercise by walking or riding in the open air, and obtain eight to 12 hours of sleep each night. Physios recommended the use of plain foods, including well cooked grains, raw and stewed fruits, pure milk, garden vegetables (except the Irish potato and tomato), small portions of beef and mutton, occasional use of fish and fowl, and the avoidance of tea, coffee, and chocolate. In addition, they prescribed vapor and water baths, drinking large amounts of water, and taking frequent enemas. In treating phthisis successfully they administered leptandra, hydrastis, iris or euonymus, combined with disoreia, zingiber, capsicum, or xanthoxylum for the lungs; decoctions of tamarac or pine bark for the throat and chest organs; and slippery elm, gum arabic or comfrey, combined with lobelia herb, capsicum, and licorice root to keep the air passages moist.^{29,30}

John Albert Burnett listed thirty remedies as the most useful and popular among the physio-medicalists in the 19th century. These included: lobelia, capsicum, bayberry, chionanthus; an antiperiodic made by taking fluid extracts of gentian and hydrastis, cascara, salicin, myrrh, and simple syrup; tincture myrrh compound; Thomsons composition; neutralizing cordial; scutellaria; asclepias; dioscorea; stillingia; crawley; sodium chloride; euonymus; fleabane; calcium lactophosphate; cimicifuga; sodium salicylate; cactus; magnesium sulphate; iron ferrocyanide; iron sulphate; zinc oxide; polemonium reptens; amphiachyris dracunculoides; echinacea; corn silk; iron salicylate; and zingiber. In 1869, quinine received the physios approval. Until its inclusion in William H. Cooks *Physio-Medical Dispensatory* of that year,

it had remained on the index of non-sanative poisons.^{32(p149)} However, some stalwarts were never quite satisfied with its inclusion and chose hydrastis canadensis as the best general tonic.³³

Other popular remedies included castor oil, wormseed oil, anise oil and tincture of myrrh for a vermifuge; valerian root, ginger root, cinnamon bark, anise seeds, prickly ash berries, and oil of sassafras as antispasmodic aromatic drops; popular bark, golden seal, bayberry, columbo root, capsicum, and cloves for bitter tonic; mandrake root, black root, blood root, gamboge, lobelia seeds, and cayenne as vegetable cathartic pills; and mayweed flowers, smartweed, bitter archangel, bittersweet, wormwood, and cayenne pepper as nerve ointment. As an alternative to opium and its derivatives, the physios recommended blue cohosh, mullen, bugle weed, coker burr, greek valerian, twin leaf, and yellow popular. For treating specific conditions, they applied the following:

Asthma. Skunk cabbage in doses of a half or whole teaspoonful, repeated as occasion required, and which acted as an antispasmodic and expectorant; and lobelia given in half or whole teaspoonful doses of the pulverized seeds or leaves and pods, at bedtime, or with the onset of fits; or smoking the dried roots of the common henbane (*Datura stramonium*) which acted as an antispasmodic and expectorant.

Nose-bleed. A snuff made from the leaves of witch hazel, and inhaled into the nose to stop the bleeding; a tea of hazel with the addition of cayenne taken internally; and the powder of charcoal as a styptic in hemorrhages from the nose.

Bleeding From the Lungs. Taking freely of diaphoretic powders to promote perspiration; a tea of witch hazel or beth root; vapor bath and emetic.

Bloody Urine. Vapor bath and emetic, followed by the use of witch hazel, beth root, and other astringents.

Cancer. A tea of pipsisway, wild lettuce, narrow dock root; the application of cat-skins or the flesh of fresh killed chickens to the open ulceration; angle-worms, or fish worms, snails, frogs and toads to be laid on an ulceration alive, and remain until they became dead and putrid.

Consumption. The tincture of lobelia, in nauseating doses, root of the skunk cabbage in half to whole teaspoonful doses.

Diarrhea. A few doses of tincture of myrrh, diaphoretic powders, bitter tonic, bayberry, or any of the astringent articles, or a cholera syrup. In addition use a butternut syrup, black root, bitter root, rhubarb, or any other cathartic.

Piles. Tincture of myrrh, or the juice of smart weed, and the administration of a stimulating injection; a salve made by simmering the bruised leaves of the Jamestown weed or henbane, in fresh butter or hogs lard, and rubbed into the affected part.

Cholera. Administering tincture of myrrh and bayberry, cholera syrup or mixture; decoction of wild-cherry bark; eat tail flag root boiled in milk or any other astringent article; with diaphoretic powder or cayenne to promote perspiration.

Costiveness. Graham bread, ripe apples, peaches, prunes and grapes, cranberries, and stewed pumpkin.

Hysteria and Convulsions. Ladyslipper, sculcap, blueberry, asafoetida, formed into pills with dandelion extract.^{23(pp23,24,28,33,42,43,54,138,39,180-182)30,35}

The physios divided on the use of alcohol in their medicines. From all the evidence before us from Noah

down to the present, observed A. H. Baird in 1882, "alcohol has cursed every family, tribe and nation, directly or indirectly, and the thousands of articles discovered for medicines have but increased its use, and following it is an increase of drunkenness, premature deaths, all of which clearly proves that medicated alcohol is not inert but however masked. . . is a fiend infernal."³⁶ Others, not so hostile, chose to employ alcohol as an essential ingredient in their drugs.

Vegetable medicines remained popular among both regular and sectarian physicians in the 19th century. A study of prescriptions in 1854 indicated that in Burlington, New Jersey, three regular physicians called for 179 different items in their 443 prescriptions written between December 1853 and March, 1854. Of that number, 105 were vegetable, 58 chemical, 7 mineral, 5 animal, and 4 proprietary. The most commonly prescribed drug of vegetable origin was opium, followed by ipecac, camphor, squill, acacia, cinchona, and rhubarb. Among the chemicals and minerals, calomel and mercury were foremost in the list of prescriptions. Although there was little polypharmacy evident in the prescriptions of these three physicians, the majority of items were liquids, followed by powders, pills, ointments, colloids, liniments, plasters, and miscellaneous items such as bark, cerate, and seeds.

KNIGHTS OF THE LOBELIA-POD

Lobelia (otherwise known as emetic weed, Indian tobacco, puke weed, gagroot, eyebright, vomitwort, and bladder-pod), official in all editions of the *US Pharmacopoeia* from 1820 to 1910, and named in honor of the English botanist Mathias de Lobel, was a plant six to twenty inches in height, with small, numerous delicate blue flowers. The plant was annual in the warm latitudes but biennial in the midwest and northeastern states, and all parts of it were considered medicinal. Its use caused a deep and bitter fight between the botanics and allopathic physicians, with the latter often condemning the plant as a poison. Most allopathic authors of herbal medicines attributed lobelia's introduction to Reverend Manasseh Cutler of Massachusetts who, writing about the plant in the *American Academy of Science* in 1785, claimed to have cured himself of asthma by its use.³⁸ This was followed by an article in 1787 which incorrectly ascribed astringent properties to the plant. According to pharmacist John Uri Lloyd, this occurred when the author confused the properties of lobelia inflata with those of a related plant known as lobelia syphilitica.^{39(p184)} Several decades later, James Thacher, in his *American New Dispensatory*, published in 1817, attributed its introduction to the Penobscot Indians in New England. Morris Mattson in his *American Vegetable Practice* (1841) also reported that lobelia inflata was used by the Penobscot Indians and as a domestic remedy by the people of New England long before its discovery by Samuel Thomson. However, valid these conflicting claims might be, Thomson employed lobelia as early as 1773 to produce vomiting and popularized the plant as a medicinal agent. By 1791, he used it regularly for colic, rheumatism, scarlet fever, erysipelas, dropsy, and other complaints in his practice which spanned Vermont, New Hampshire, New York, and Massachusetts.^{40(pp519-521),41} The many preparations of lobelia included the following:

1. Infusion (drachm to half pint of water): Used for emetic purposes, to secure full relaxation in rheumatic or convulsive situations, or for dislocations.
2. Extract (bruising the green herb and macerating it with diluted alcohol): Used to create a relaxing influence in febrile and acute rheumatic situations; sometimes used as a plaster for irritation of the spine.
3. Fluid Extract (lobelia herb macerated in alcohol and acetic acid): Used frequently as an expectorant and nauseant.
4. Tincture (crushed lobelia herb, including the seeds, and diluted alcohol): Used in cases of acute pleurisy, pneumonia, rheumatism, and spasmodic croup.
5. Acetous Tincture (lobelia seeds, well ground, with distilled vinegar and diluted alcohol): Acts on the respiratory organs as a relaxant and stimulant, promoting rapid expectoration and relaxing spasms.
6. Acetous Syru (acetous tincture dissolved in white sugar): Employed for same situations as acetous tincture.
7. Oxymel, Honey of Lobelia (tincture of bruised lobelia herb in cider vinegar and clarified honey): Used for dry and irritable coughs; less stimulating and more soothing than the acetous preparations.
8. Oil (pulverized seed with sulphuric ether): Given in five drop doses as an emetic. Lozenges (acetous tincture and white sugar): A relaxing expectorant for irritable coughs.
9. Lozenges (acetous tincture and white sugar): A relaxing expectorant for irritable coughs.
10. Compound Tincture of Lobelia and Capsicum, Antispasmodic Tincture, Thomson's Third Preparation (lobelia seeds and capsicum, cypripedium, and compound tincture of myrrh): Used as powerful stimulating and relaxing compound; arouses the stomach, the circulation, and the nervous system.
11. Balsam of Honey (tincture of lobelia, essence of anise and of sassafras, and clarified honey): Effective expectorant and antispasmodic in whooping-cough and dryness of the air passages.
12. Compound Pills (lobelia seeds, cypripedium, asarum, and softened extract of boneset): Used as a mild nauseant and expectorant; valuable in nervousness, mild hysteria, neuralgia, nervous headache, and sleeplessness.
13. Stomach Pill (lobelia seeds, apocynum, hydrastis and capsicum): Used for chronic atony of the stomach and in cases of dropsy and atonic forms of digestion.
14. Suppositories (lobelia seeds, simple cerate, and pulverized gum Arabic): Used for all acute pains of pelvic region and lower bowels, and especially for restlessness, chronic ovaritis, sciatica, neuralgia, and rheumatism of the womb.^{40(pp543-545),41}

Regular medical journals published numerous accounts of the effects of lobelia. Parke, Davis and Company reported in 1893 that it was a vaso-motor poison and referred to several convictions for manslaughter. Much of this discussion had resulted from the notoriety of a murder trial in 1809 when Thomson was tried before the Supreme Court in Salem, Massachusetts, for the murder of Ezra Lovett, Jr, by poisoning with lobelia. Although Thomson was acquitted, the case was subsequently cited in most allopathic texts to document and stereotype the drug's dangerous effects. In explaining these instances of alleged poisoning, the physios emphasized the possibility for impurities, raised questions of whether the seeds or leaves had been used, and suggested that the constitution of the patient might not have been assessed carefully in judging the size of the dose. Despite negative publicity, lobelia remained the most important medicine of the Thomsonians and physios.⁴²

PHYSIO-PHARMACY

The early botanics refused to purchase their medicines from pharmacists, fearing adulteration with mineral poisons and objecting on democratic grounds to the secrecy involved in the use of Latin in prescription-writing. More importantly, however, botanics wished to control their own drug trade which meant either making their own medicines or purchasing them from their own firms. Among the early

PHYSIO-MEDICAL DRUG HOUSE.

C. T. BEDFORD

PHYSICIANS' SUPPLIES,

No. 2 Indiana Avenue, INDIANAPOLIS, IND.

SOME OF OUR SPECIALTIES.

Containers Included when not Specified.

Syr. Rhei et Potass. Comp., Double Strength—Prof. Hasty's Formula.
Syr. Myrica Comp.—Thomson's Formula.
Syr. Mitchellia Comp., Improved.
Syr. Solidago Comp.—Prof. Davidson's make.
Syr. Fraxinus Comp.—Cook's Formula.
Syr. Juglans Cin.—Prof. Davidson's make, new crop.
Fld. Ext. Solidago Comp.—Prof. Davidson's make.
Fld. Ext. Geum Album—Prof. Davidson's formula.
Fld. Ext. Composition—Thomson's Formula.
Physio-medical C. C. Pill—Prof. Hasty's Formula.
Physio-medical C. C. Pill—Stimson's manufacture.
Po. Composition—Thomson's Formula.
Po. Spice Bitters.
Po. Populus Comp.—Cook's Formula.
Anti-bilious Comp.—Prof. Anthony's Formula.
Neutralizing Mixture—Prof. Anthony's Formula.
Bedford's Sore Throat Mixture.
Bedford's Pile Suppositories.
Prof. Anthony's Cath. Pills.
Tinct. Lobelia Comp. (3d prep.).
Tinct. Myrrh Comp. [No. 6]—Thomson's Formula.
Oil Lobelia—Prof. Davidson's make.
Oil Capsicum—Prof. Davidson's make.
Salicylate of Soda. Free from carbolic acid—Schieffellins.

Just received a fresh supply of Syrup Juglans made from the green bark by Prof. Davidson. It is full strength and well made, a pint of the syrup representing a pound of the bark and warranted to give satisfaction.

We handle Wm. S. Merrell's Fluid Extracts, Syrups, Elixirs, Reisinoids, etc.

FIGURE 4. Advertisement for drugs from a physio-medical drug course, 1890.¹⁶

botanical pharmacists was John Thomson (son of Samuel Thomson) who owned a wholesale and retail house in New York City for users of herbal medicines; Godfrey Myer and Company of Columbus, Ohio; Ward Sears and Company of Baltimore; John Burns Milford Thomsonian Depot in New Hampshire; Westerfield Pharmaceutical Company of Dayton, Ohio; and the New England Thomsonian Depot of D. L. Hale in Boston.²²

Following the decline of the Old Thomsonians, the physios lacked sufficient numbers to sustain their own drug manufacturing firms. Instead they relied on the good will of the eclectic pharmaceutical industry which advertised in physio-medical journals and offered a long line of "concentrated" preparations for reform and "new school" physicians. Among them, the products of the eclectic pharmacist John Uri Lloyd of Cincinnati were highly favored by physios everywhere. Physios also purchased their "concentrated tinctures" from B. Keith and Company, of New York City; F. D. Hill and Company in Cincinnati; Jacob S. Merrell of St Louis; Coolidge and Adams of New York; and a physio-medical druggist named Bedford in Indianapolis (Fig 4).^{27(p146)} Parke, Davis, and

Company of Detroit, Michigan, introduced a number of botanic remedies which were praised by the physios as sanative, efficient, and valuable. These included coto bark used as an astringent in diarrhea and dysentery; tonga, a Fijian remedy for neuralgia; and lippia Mexicana, and expectorant. Abbott Alkaloidal Company of East Ravenswood Park, Chicago, also advertised its medicines in physio journals as did the William S. Merrell Chemical Company (eclectic) of Cincinnati which sold "specific tinctures" along with corn silk, saw palmetto, black haw, echinacea, black cohosh, cactus, passion flower, cotton root bark, fringe tree, and stone root.^{43,44}

The physios also praised the pharmaceutical firm of Eli Lilly and Company of Indiana because of the care of its employees took in selecting drugs that were pure and fresh.⁴⁵ "Honesty, industry, and energy has made Mr Lilly the pill man of the country," remarked the editor of the *Physio-Medical Journal* in 1881. Lilly sold a number of sugar coated herbal pills to the physio-medicals, including their Ague Physio-Medical, Apocynin Compound, Cohosh Compound, Lobelia Compound, and Podophyllin Compound.⁴⁶

However grateful the physios were to the industrial pharmacist for the sale of botanic medicines, they never fully accepted the absence of companies devoted exclusively to their own medicinal needs. This remained a long-standing embarrassment as well as a serious impediment to their growth in the 19th century. Many physios simply refused to compromise on their principles, preferring instead to prepare their own medicines. "But I may save your money, and time, and patients, and make your own preparations from the drugs that you have handled yourself," advised Melville C. Keith, MD, in 1887.^{27(p146)}

The gathering and preservation of medicinal herbs, roots, and barks required knowledge of the proper seasons, judicious selection, and careful processing. Annual roots which grew from seed each year were gathered just before flowering; biennial roots were gathered in the fall of the first year, or early in the spring of the second. Triennial roots were collected in the fall of the second year, or spring of the third year; while perennial roots were collected either in the fall after the leaves and tops began to die, or in the spring before they began to grow. After the roots were collected and before they dried, they had to be washed and trimmed of extraneous material. Roots could not remain long in water because of the danger of losing essential virtues. After washing, the roots were cut into small pieces and spread out to dry in an airy place or in sunshine. Again, care was taken to prevent their becoming wet. When dry, they were packed in jars, boxes, or barrels according to their quantity and placed in a dry, airy room. Leaves were gathered at the time of flowering since they were at their peak then. They were dried with the same precautions as roots, and preserved in a similar manner. Barks were gathered in spring or all, carefully dried, and preserved in a fashion similar to roots and herbs. Flowers were collected when about to open from the bud, or in a state of full perfection, in dry weather, and carefully and quickly dried in shade, and preserved as the others.^{23(pp409-411),47(pp58,59)}

GERM THEORY

The germ theory of disease causation brought a period of excitement to the 1880s and 1890s. Robert Koch's (1843-1919) description in 1876 of the life-history of the bacillus of anthrax elevated germ theory to a scientific basis. His discovery of the *Mycobacterium tuberculosis* and his identi-

cation of the cholera bacillus in 1882, and the findings by scientists in subsequent years challenged many of medicine's long held beliefs by linking a specific organism with a specific disease. Koch's "postulates" for the diagnosis of disease became the anchor of bacteriology and, despite the confusing basis upon which his evidence rested set doctors and scientists scurrying to embrace the theory, adapt it to older theories, or oppose it as contrary to the principles of medicine.⁴⁸⁻⁵¹

"It is a strange fact," remarked M. Hermance, MD, writing in the *Physio-Medical Journal* in 1895, "that physicians of all schools, except the physio-medical, have always held to some erroneous theory as to what constitutes disease and its causes." Across the profession, medical scientists were beginning to replace the erroneous malarial theory of disease with an equally erroneous germ theory. Before long, he predicted, those same scientists would be suggested that malaria was an undiscovered microbe. Hermance argued that the bacillin tuberculosis which regulars had discovered to be the cause of tuberculosis was, in fact, the condition rather than the cause of the condition. "I have come to the conclusion," he wrote, "that instead of microbes, bacilli or whatever name they may be called, being the cause of disease, they are in and of themselves harmless, but the menstrum in which they are developed and live, constitutes the poisonous element which is capable of producing the disease in others, if the disease is not of a contagious nature." For the physios, this meant that anything that deprived the organs of their ability to perform normal functions became the cause of disease.^{52(pp37,42)}

Hermance was not unlike the majority of practicing physios who continued to believe that the most rational explanation of disease causation had come from John Thomson's work on Asiatic cholera, published some sixty years earlier. Thomson attributed Asiatic cholera to the "unusual destruction of animal and vegetable matter during violent and sudden changes in the weather," and the "excess of nitrous or morbid gas that was extracted by the power of heat from the decaying mass during the summer weather."^{52(pp94,97,100,101)} Even after 60 years, Hermance insisted that Thomson's theory was the most sensible ever advanced to explain the cause of cholera and was surely a fuller explanation than the microbe theory then in vogue. He further believed that Thomson's explanation applied as well to germ theory, namely, that "all the microscopical animalcula ever found in the excretions or fluids of the body in a person diseased are the result of disease, and not the cause of it."^{52(p104)}

The physios continued in the main to be "bug cranks," believing that bacteria was "a good thing to have in a wound when they live by their own pabulum." J. M. Thurston of the Physio-Medical College of Indiana admitted to having experimented with antiseptics but found they were too strong. Instead, he reverted to the use of Thomson's Rheumatic Drops (known popularly as No 6), arguing that the "best antiseptic is vital force."^{53(p163)} There could never be too high an importance placed on the vital vigor preparatory for the ordeal of surgery. Excessive catharsis, or any form of depletion, would detract from the vital force in the tissue-unit. In this regard, the physios preached their own special brand of conservative surgery.^{21(p303)}

Overall, the physios took exception to the germ theory, calling Koch the "great German Baccilio-Manic" and a "would-be scientist."⁵⁴ More specifically, they criticized germ theory because it lacked a working hypothesis based

on the immutable laws of physiology. Until medicine returned to a more rational foundation, all of its vaunted progress and advanced methods, including bacteriology, would remain but "a splendid conglomerate of experimental concrete facts" and aimless empirical applications.^{21(pp8,9)} Most physios concurred with the comment made in 1907 by a professor at the Physio-Medical College of Indiana that "the so-called 'disease germ' is a monumental medical bugbear, it is the greatest romanticism of the age."^{32(p150)}

In spite of frequent reference to bacteria, tissue-units, bioplasm, and other more modern terminology, the physio-medicalists continued to rely on the regimens handed down by Samuel Thomson and other early advocates of herbal medicines, including naturalist Constantine Smaltz Rafinesque (1784-1841), physician James Thatcher (1754-1844), botanist Jacob Bigelow (1786-1879), and physician and naturalist Benjamin Smith Barton (1766-1815). This meant the importance of maintaining an "aseptic state" for the gastro-intestinal tract with the use of sodium salicylate, potassium chlorate, potassium nitrate, acid borate, acid citric, and acid tannic. The most popular vegetable antiseptics included baptisia, oleum cinnamomum triturated with sugar of milk or boric acid, and erythroxylon coca.^{21(p106)} The physios also employed mints, balms, lobelias, vapor-baths, spongings of water, and other sanative means, including electricity and magnetism, to "loosen the tissues, open the emunctories and make a way of escape to any and every deleterious matter that may exist in the system." This was a system based on "simplicity, truthfulness, and safety."⁵⁵

RETROSPECT

The physios were especially strong in Ohio, Indiana, Illinois, and Iowa, with additional followings in Texas, Oregon, and Washington. At their peak, probably no more than 2,500 physicians were practicing this form of medicine at any one time. Even this number is inflated since the national organization, formed in 1883, claimed only 150 members. According to an eclectic survey in 1894, the regulars numbered 72,028; the eclectics, 10,292; the homeopaths, 9,648; and the physios, 1,553.⁵⁶ On average, physio-medical colleges graduated 21.6 physicians annually between 1881 and 1890. Of the state societies, Indiana was the oldest, having organized in 1863; others were in Ohio, Illinois, Iowa, Michigan, and Washington.^{22(p152)} In 1900, the *Ohio Medical Directory* listed 1,162 sectarians practicing in the state. This amounted to nearly 19% of all physicians; of that number, 769 were homeopaths, 342 were eclectics, 41 were physio-medicalists, and 7 were minor cultists. By 1905, the percentage of sectarians had declined to 17% and, by 1917, they represented only 13% of the practicing physicians in the state. In 1938, there were fewer than 160 sectarians practicing in Ohio, or 1.75% of the total number of practicing physicians.⁵⁷

REFERENCES

1. Harold CN: Alumni address. *Physio-Medical Journal* 1886; 12:215.
2. Rothstein WG: Botanical Movements and Orthodox Medicine, in Gevitz N (ed): *Other Healers: Unorthodox Medicine in America*. Baltimore, Johns Hopkins University Press, 1988, pp42-45.
3. Anthony E: Physio-medicalism and progress. *Physio-Medical Journal* 1886; 12:227-233.
4. Ball JM: Samuel Thomson (1769-1843) and His Patented "System" of Medicine. *Annals of Medical History* 1925; 7:144-149.
5. Waite FC: Thomsonianism in Ohio. *Ohio State Archaeol Hist Quart* 1940; 49:322-331.
6. Johnson WL: To the editor. *Thomsonian Recorder* 1837, vol 1, p228.
7. Curtis A: *A Fair Examination and Criticism of All the Medical Systems in Vogue*. Cincinnati, printed for the Proprietor, 1865.

8. Thomson S: *New Guide to Health; Or, Botanic Family Physician, Containing a Complete System of Practice on a Plan Entirely New: With a Description of the Vegetables Made Use of, and Directions for Preparing and Administering*. Boston, J. Howe, 1825.
9. Berman A: The Thomsonian Movement and Its Relation to American Pharmacy and Medicine. *Bull Hist Med* 1951; 25:405-428; 519-538.
10. Forman J: Dr. Alva Curtis in Columbus, the Thomsonian Recorder and Columbus' First Medical School. *Ohio State Archaeol Hist Quart* 1942; 51:332-340.
11. Breeden JO: Thomsonianism in Virginia. *Virginia Magazine of History and Biography* 1974; 82:150-180.
12. Forman J: Dr Alva Curtis in Columbus. *Ohio State Archaeol Hist Quart* 1941; 50:373-379.
13. Curtis A: Remarks. *Thomsonian Recorder* 1837; 5:229.
14. Curtis A: Botanico-Medical School. *Thomsonian Recorder* 1836; 5:30.
15. Robinson S: *A Course of Fifteen Lectures, on Medical Botany, Denominated Thomson's New Theory of Medical Practice*. Columbus, Ohio, Horton Howard, 1829.
16. Rafinesque CS: *Medical Flora; or, Manual of the Medical Botany of the United States of North America*, 2 vols, Philadelphia, Atkinson and Alexander, pp1828-1830.
17. Barton BS: *Elements of Botany; or, Outlines of the Natural History of Vegetables*. Philadelphia, printed for the author, 1803.
18. Eaton A: *Manual of Botany for North America: Containing Generic and Specific Descriptions of the Indigenous Plants and Common Cultivated Exotics, Growing North of the Gulf of Mexico*. Albany, Webster and Skinner, 1829.
19. Juettner O: *Daniel Drake and His Followers: Historical and Biographical Sketches*. Cincinnati, Harvey Publishing Co, 1909.
20. Anonymous: An Address to the Public. *Physio-Medical Journal* 1883; 9: 184.
21. Thurston JM: *The Philosophy of Physiomedicalism. Its Theorem, Corollary, and Laws of Application for the Cure of Disease*. Richmond, Indiana, Nicholson Printing and Manufacturing Company, 1900.
22. Nichols JB: Physiomedicalism. *Medical News* 1895; 66:153-154.
23. Howard H: *An Improved System of Botanic Medicine Founded Upon Correct Physiological Principles; Comprising a Complete Treatise on the Practice of Medicine*. Cincinnati, Kost, Bigger and Hart, 1854.
24. Broady FO: A medical practice without alcohol and without poisons. *Physio-Medical Record* 1903; 6:261.
25. Brown OP: *The Complete Herbalist; or, the People Their Own Physicians by the Use of Nature's Remedies*. Jersey City, New Jersey, published by the author, 1872.
26. Hoener FG: Herbal medicines. *Physio-Medical Journal* 1887; 13:22-23.
27. Keith MC: The remedies we use. *Physio-Medical Journal* 1887; 13:144-46.
28. Curtis A: *A Fair Examination and Criticism of All the Medical Systems in Vogue*. Cincinnati, printed for the proprietor, 1865.
29. Baird AH: Phthisis pulmonalis. *Physio-Medical Journal* 1890; 16:33-42.
30. Editor: American Association of Physio-Medical Physicians and Surgeons—Eleventh annual session. *Physio-Medical Journal* 1893; 19:209.
31. Burnett JA: A selection of thirty physio-medical remedies. *Physio-Medical Record* 1906; 9:124.
32. Berman A: Neo-Thomsonianism in the United States. *J Hist Med* 1956; 10:133-55.
33. Harold NE: The best physio-medical tonic. *Physio-Medical Record* 1905; 8:123-25.
34. Anonymous: Hygiene for costiveness. *Oregon Physio-Medical Journal* 1867; 2:97-99.
35. Anonymous: Nervine pills. *Oregon Physio-Medical Journal* 1867; 1:64.
36. Baird AH: Alcohol. *Physio-Medical Journal* 1882; 8:310-11.
37. Cowen D, King LD, Lordi NG: Nineteenth century drug therapy: Computer analysis of the 1854 prescription file of a Burlington pharmacy. *J Med Soc NJ* 1981; 78:758-61.
38. Cutler M: Account of indigenous vegetables. *Amer J Sci Arts* 1785; 484.
39. Lloyd JU: *Origin and History of All the Pharmacopeial Vegetable Drugs*. Cincinnati, Caxton Press, 1929.
40. Cook WH: *The Physio-Medical Dispensatory: A Treatise on Therapeutics, Materia Medica, and Pharmacy*. Cincinnati, published by author, 1869.
41. Thacher J: *The American New Dispensatory: Containing General Principles of Pharmaceutic Chemistry; Chemical Analyses of the Articles of Materia Medica; Pharmaceutic Operations; Materia Medica*. Boston, Thomas B. Wait and Sons, 1817.
42. Simmons J: Is lobelia a poison? *Physio-Medical Journal* 1893; 19:40-41.
43. Thurston JM: Agree to not agree. *Physio-Medical Journal* 1882; 8:120.
44. Anonymous: Coto bark. *Physio-Medical Journal* 1890; 7:59.
45. Anonymous: Eli Lilly and Co. *Physio-Medical Journal* 1890; 16:126.
46. Anonymous: The great pill maker. *Physio-Medical Journal* 1881; 7:61.
47. Lyle TJ: *Physio-Medical Therapeutics, Materia Medica, and Pharmacy*. Salem, Ohio, J. M. Lyle and Bro, 1897.
48. Buerki RA: The reception of the germ theory of disease in the *American Journal of Pharmacy*. *Pharm Hist* 1971; 13:158-68.
49. Lechevalier HA, Solotorovsky M: *Three Centuries of Microbiology*. New York, McGraw Hill, 1965.
50. Crellin JK: The dawn of germ theory: particles, infection, and biology, in Poynter FNL (ed): *Medicine and Science in the 1860's: Proceedings of the Sixth British Congress on the History of Medicine*. London, Wellcome Institute of the History of Medicine, 1968, pp57-76.
51. Bulloch W: *The History of Bacteriology*. London, Oxford University Press, 1938.
52. Hermance M: The germ theory of disease—Is it true or false? *Physio-Medical Journal* 1895; 21:37-42; 94-104.
53. Editor: Proceedings of the 32nd annual session of the Physio-Medical Association. *Physio-Medical Journal* 1895; 21:160-63.
54. Editor: At it again. *Physio-Medical Journal* 1882; 8:253-54.
55. Shelton JC: Application of the fundamental principles of medical science to clinical practice. *Oregon Physio-Medical Journal* 1866; 1:100-101.
56. Anonymous: Statistics. *Eclectic Medical Journal* 1894; 44:396.
57. Waite FC: Sectarian medicine in Ohio. *Ohio St Med J* 1953; 50:48-51.

Diagnosis of occult primary rhabdomyosarcoma by magnetic resonance imaging

NEIL M. ROFSKY, MD; NANCY B. GENIESER, MD; MICHAEL M. AMBROSINO, MD; JEFFREY C. WEINREB, MD; KEVIN ROCHE, MD; AARON R. RAUSEN, MD

Magnetic resonance imaging (MRI) may be helpful in diagnosing the presumed site of primary rhabdomyosarcoma presenting as metastatic disease. In this report, we describe two patients in whom the site of the primary tumor was unknown and was delineated with MRI.

CASE REPORTS

Case 1. An 11-year-old boy presented with a three-week history of low-grade fevers, a 10-lb weight loss, fatigue, and night sweats. An initial chest radiograph demonstrated a large, left pleural effusion, a right hilar mass, and nodules in the right lung. Work-up for an infectious etiology was negative; a neoplastic process was considered. On subsequent physical examination, a subtle, bruised appearance of the left heel was noted with no palpable mass. A history of irritation to this area, attributed by the parents to a tightly fitting ski boot worn two weeks prior to admission, was elicited. This bruise failed to disappear. MRI revealed a 3.1×2.1 -cm soft tissue mass posterior to the achilles tendon (Fig 1). A fine-needle aspirate was consistent with rhabdomyosarcoma. A pleural biopsy confirmed metastatic disease.

With informed consent, the patient was started on chemotherapy following the protocol of the Intergroup Rhabdomyosarcoma Study IV for Clinical Group IV Disease (Children's Cancer Study Group protocol no 6881). Initial chemotherapy consisted of two cycles of intravenous ifosfamide and doxorubicin given three weeks apart. With no response, chemotherapy was switched to six weekly injections of intravenous vincristine and two cycles of intravenous actinomycin D and cyclophosphamide, given three weeks apart. In spite of this therapy and a subsequent cycle of intravenous cisplatin and etoposide, pulmonary metastatic disease progressed

and the patient died 13 weeks after the initiation of chemotherapy.

Case 2. A 14-year-old female presented with a two-week history of low back pain and consequent difficulty in ambulation. Plain films of the spine revealed multiple collapsed lumbar and thoracic vertebral bodies. On physical examination, a painless 2-cm soft tissue mass was noted posterior to the metatarsal heads on the plantar surface of the right foot. The patient attributed this mass to a presumed bee sting sustained while at summer camp three months prior to admission. This mass had slowly grown in size. An MRI study of the feet demonstrated a 2.4×1.6 -cm soft tissue mass at the plantar surface of the right foot (Fig 2). A metastatic bone survey revealed destruction of the medial border of the scapula. An incisional biopsy of the scapula lesion confirmed a diagnosis of rhabdomyosarcoma. Rhabdomyoblasts were also present in a posterior iliac crest marrow aspirate and biopsy.

With informed consent the patient was started on chemotherapy following the proto-

col of the Intergroup Rhabdomyosarcoma Study III for Clinical Group IV Disease (Children's Cancer Study Group Protocol no 631). Initial intravenous combination chemotherapy included vincristine, cisplatin, doxorubicin, and cyclophosphamide. Within two weeks, her back pain had subsided, a marrow aspirate was devoid of tumor cells, and the mass lesion in the foot was half its original diameter. Combination chemotherapy with the same agents was continued with the addition of intravenous actinomycin D and a short course of etoposide after five months of therapy. At this time, the foot lesion was gone on physical examination and repeat MRI. Marrow biopsy was still positive for rare tumor cells. Combination chemotherapy was continued.

Marrow biopsies became negative after ten months of chemotherapy but again demonstrated tumor on a routine monitoring biopsy obtained after 22 months of therapy. Chemotherapy was changed to cycles of intravenous ifosfamide and etoposide, with reversion to negative monitoring marrow biopsies. A routine monitoring MRI of the right foot revealed local recurrence 42 months after diagnosis.

Excisional biopsy of the foot lesion and the use of intensive combination chemotherapy including intravenous vincristine, actinomycin D, cisplatin, etoposide, and melphalan could not control local recurrence in the right foot. A further attempt to control the recur-



FIGURE 1. Sagittal MRI scan of the foot (0.5 Tesla field strength: SE, TR 500 msec, TE 30 msec). A soft tissue mass (white arrows) is noted posterior to the Achilles tendon with low signal intensity relative to adjacent subcutaneous fat. Rhabdomyosarcoma was diagnosed with needle aspiration.



FIGURE 2. Coronal MR scan of the foot (0.5 Tesla field strength: SE, TR 900 msec, TE 60 msec). A soft tissue mass (black arrows) with low signal intensity relative to adjacent subcutaneous fat is located at the plantar surface.

From the Departments of Radiology (Drs Rofsky, Genieser, Ambrosino, Weinreb, and Roche) and Pediatrics (Dr Rausen), New York University Medical Center, New York, NY.

Address correspondence to Dr Rofsky, MRI, New York University Medical Center, 530 First Ave, New York, NY 10016.

rence with intensive local radiation combined with intensive chemotherapy and autologous marrow rescue was unsuccessful. Ultimately an above the ankle amputation was performed with the use of an artificial prosthesis for palliation. Pulmonary metastatic disease ensued and resulted in death 55 months after diagnosis.

DISCUSSION

Soft tissue sarcomas are relatively rare tumors, accounting for 1% of malignant neoplasms.¹ Rhabdomyosarcomas are among the more common ones within this group, accounting for approximately 20% of lesions.¹ They usually present as soft tissue masses. Their malignant nature frequently is not appreciated when first noted.

In these two cases, the presumed site of origin of the tumor by both history and physical examination was serendipitous. The clinical presentations were manifestations of widespread metastatic disease, consistent with the tendency of soft tissue sarcomas to demonstrate early hematogenous dissemination. Despite the frequent association with a history of recent trauma, as was the case in both of these patients, there is no known etiologic relationship between trauma and these tumors.²

MRI signal characteristics are not specific in distinguishing benign from malignant disease nor in determining the histologic etiology.³ Signal characteristics depend on the type of tissue that the tumor contains and the corresponding fractions of water, fat, fibrous

tissue, tumor cells, and blood.⁴ Lesions located within muscles or in the intramuscular septa are best seen with T₂-weighted imaging sequences, whereas those located in the subcutaneous fat are best delineated with T₁-weighted imaging sequences.⁵ Both pulse sequences should be employed in the evaluation of soft tissue masses.

MRI has proven to be superior to computed tomography (CT) in the evaluation of soft tissue tumors.^{6,7} This was particularly well demonstrated in a recent prospective evaluation of MRI and CT in 40 patients with primary soft tissue sarcomas of the extremities by Demas et al.⁶ In that study, 23% of MRI studies showed tumor involvement in one or more individual muscles that appeared normal on CT scans. In addition to aiding the localization of an occult primary tumor, MRI, by virtue of its ability to delineate more clearly the extent and margins of lesions, may affect the determination of radiation ports and surgical resection margins.⁷

MRI is also valuable in the assessment of musculoskeletal tumors following therapy.^{8,9} In the second case, MRI demonstrated recurrent tumor when this was not apparent clinically and when the monitoring marrow specimens were negative. In this case, the MRI study provided the information to recommend surgery and altered chemotherapy. It remains to be seen whether MRI can reliably demonstrate tumor recurrence at an earlier time compared with other methods for monitoring soft tissue tumors. This possibility could allow for earlier institution of treatment and improved outcomes.

In a child presenting with systemic manifestations of metastatic disease, occult soft tissue sarcomas should be considered, and careful attention to vague signs or symptoms in the extremities should prompt evaluation with MRI. Although non-specific, a soft tissue mass identified by MRI may provide a readily accessible site for needle aspiration or biopsy.

REFERENCES

1. Enterline HT: Histopathology of sarcomas. *Semin Oncol* 1981; 8:133-135.
2. Chang AE, Rosenberg SA, Glatstein EJ, et al: Sarcomas of soft tissues. In Devita VT Jr, Hellman S, and Rosenberg SA, (eds): *Cancer Principles and Practice of Oncology*, ed 3, Philadelphia, JB Lippincott Company, 1989, p1346.
3. Kransdorf MJ, Jelinek JS, Moser RP Jr, et al: Soft tissue masses: diagnosis using MR imaging. *AJR* 1989; 153: 541-547.
4. Petterson H, Slone RM, Spanier S, et al: Musculoskeletal tumors: T1 and T2 relaxation times. *Radiology* 1988; 167: 783-785.
5. Totty WG, Murphy WA, Lee JKT: Soft tissue tumors: MR imaging. *Radiology* 1986; 160:135-141.
6. Demas BE, Heelan RT, Lane J, et al: Soft-tissue sarcomas of the extremities: comparison of MR and CT in determining the extent of disease. *AJR* 1988; 150:615-620.
7. Tehranzadeh J, Mnaymneh W, Ghavam C, et al: Comparison of CT and MR imaging musculoskeletal neoplasms. *J Comput Assist Tomogr* 1989; 13: 466-472.
8. Vanel D, Lacombe M, Couanet D, et al: Musculoskeletal tumors: follow-up with MR imaging after treatment with surgery and radiation therapy. *Radiology* 1987; 164:243-245.
9. Sanchez RB, Quinn SF, Walling A, et al: Musculoskeletal neoplasms after intra-arterial chemotherapy: correlation of MR images with pathologic specimens. *Radiology* 1990; 174:517-526.

Coronary artery aneurysms

Case report and review of the literature

TAK KWAN, MD; A. DINO PAIUSCO, MD; C. V. R. REDDY, MD; ALAN FEIT, MD

Coronary artery aneurysms characterized by diffuse or localized dilatation of the coronary arteries, have also been referred to as aneurysmal coronary artery disease¹ and coronary ectasia.²⁻⁴ They can present with atherosclerotic, congenital, inflammatory and traumatic etiologies. By far the most common cause is obstructive coronary artery disease. We describe a case of coronary artery aneurysms in a patient who suffered a myocardial infarction, and assess the clinical significance and outcome of this entity.

From the Department of Medicine, Division of Cardiology, State University of New York, Health Science Center at Brooklyn, Brooklyn, NY.

Address correspondence to Dr Kwan, Box 1199, Division of Cardiology, State University of New York, Health Science Center at Brooklyn, 450 Clarkson Ave, Brooklyn, NY 11203.

CASE REPORT

A 62-year-old woman was admitted with a chief complaint of chest pain with nausea and diaphoresis for 24 hours. She had a history of hypertension as well as stable angina for the past five years, for which she was receiving nitrates and a β -blocker.

A 12-lead electrocardiogram showed new Q waves in the inferior leads compared with an electrocardiogram done six months earlier. She was treated with the following: nitroglycerine, 10 μ m/min intravenously; aspirin, 350 mg; and metoprolol, 50 mg orally. Her pain was subsequently relieved. The peak creatine kinase level was 540 IU/L with a 20% MB fraction (normal, MB <5%).

Her hospital course was uneventful. Two-dimensional echocardiography revealed inferior wall akinesis with a normal left ventricular ejection fraction. A submaximal exercise treadmill test without thallium on day 9

showed no chest pain and no evidence of ischemia. She was subsequently discharged. Four weeks after the myocardial infarction, she again experienced typical anginal pain, for which she was advised to have coronary angiography.

Routine laboratory data showed a normal complete blood cell count and normal serum electrolyte levels. The VDRL test was non-reactive as were serum antinuclear antibody studies. A chest radiograph showed a normal cardiac silhouette and clear lung fields. Hemodynamic data revealed a central aortic pressure of 155/80 mm Hg, left ventricular end diastolic pressure of 27 mm Hg, and no gradient across the aortic valve. Coronary angiography showed fusiform aneurysmal dilatation of all epicardial arteries (Fig 1) with sluggish contrast wash out. There was total occlusion of the posterior descending artery at its origin. Left ventriculography showed an



FIGURE 1. Coronary angiogram of the left coronary artery revealing fusiform aneurysmal dilatation of the major epicardial vessels. The filling defect in the left main artery is caused by streaming and swirling of contrast inside the large aneurysmal space and should not be confused with thrombus (top). Coronary angiogram of the right coronary artery. Arrow indicates the total occlusion at the origin of the posterior descending artery (bottom).

akinetic inferior wall with an ejection fraction of 49%. She was discharged to her home on a regiment of aspirin, 350 mg once a day, metoprolol, 100 mg twice a day, and sublingual nitroglycerine as needed.

DISCUSSION

Coronary artery aneurysms were first reported by Bougon⁵ in 1812.⁵ Until 1963, only 89 cases of coronary artery aneurysms had been reported, all diagnosed by postmortem examination.⁶ With the introduction of selective coronary angiography, the antemortem

diagnosis of coronary artery aneurysms became possible.

In this patient, myocardial infarction probably resulted from an embolus arising from the proximal segment of the right coronary artery, or from a thrombus in situ at the origin of the posterior descending artery. The possibility of atherosclerotic narrowing at the origin of the posterior descending artery with acute thrombus development is less likely but could not be ruled out. Post-myocardial infarction angina was most likely caused by sluggish blood flow through the aneurysmal arteries.

From the registry data of Coronary Artery Surgery Study (CASS) (July 1975 to May 1979),¹ 978 patients were found to have coronary artery aneurysms. In patients referred for coronary angiography, the incidence was about 4.9%. Hartnell et al² reported the incidence of coronary artery aneurysms to be 1.4% among 4,993 patients who underwent coronary angiography. Other series have reported the incidence to be from 0.3% to 2.5% (Table I).

The definition of coronary artery aneurysms has varied. In Falsetti and Carroll's report,⁷ coronary artery aneurysms were defined as dilatation of the coronary artery diameter by at least two times its usual diameter over a segment of at least 2 cm in length. Swaye et al¹ required coronary dilatation that exceeded the diameter of normal adjacent segments or the diameter of the patient's largest coronary vessel by $1\frac{1}{2}\times$. Befeler et al⁸ defined it as a localized dilatation of a major vessel which exceeded the expected diameter of that section as compared to normal segments above and below.

Among patients without obstructive lesions in one study, the incidence of coronary artery aneurysms was extremely low (0.1%).¹ Rath et al⁹ reported the clinical course of five patients with aneurysmal coronary artery disease but without stenosis. All five patients developed complete occlusion of a previously non-stenosed aneurysmal vessel.

The most common cause of coronary artery aneurysms is atherosclerosis, occurring in as many as 52% of patients in some reports.⁶ Other reported causes include congenital diseases,^{10,11} rheumatic fever,¹² syphilis,¹³ polyarteritis nodosa,¹⁴ Kawasaki disease,¹⁵ as a result of blunt chest trauma,¹⁶ infection (mycotic),^{13,17} dissection of the coronary arteries,^{18,19} and following coronary angioplasty.²⁰

Coronary artery aneurysms involve the right coronary artery in about 70% of cases, the left anterior descending artery in 51%, and the left circumflex artery in 44% (Table II). The reasons for the predominance of right coro-

nary artery involvement is not clear. Topaz et al²¹ recently discussed the significance of left main artery aneurysms. They are usually associated with significant two or three vessel coronary artery aneurysms and a "filling defect" in the aneurysmal structure during contrast injections. This phenomenon is caused by streaming and swirling of contrast inside the large aneurysmal space. A diagnosis of thrombus should not be confused with this "filling defect."

The association of aneurysm with coronary artery stenosis shows a profound sex difference. Hartnell et al² reported that of the 1,051 female patients studied, 414 (39%) had significant coronary artery stenosis but only 0.5% had coronary artery aneurysms; this contrasts with the male patients, in whom 64 of 2,885 (2.2%) with coronary narrowing had aneurysms.

Tunick et al²² described coronary artery aneurysm, defined as a localized abnormal dilatation of the coronary artery that is spherical or saccular. In the 8,422 patients they studied, the incidence was 0.2%. In contrast with the diffuse type of aneurysm, the left anterior descending artery was the most frequently involved artery (68%), and discrete aneurysms were not found in patients without severe fixed stenosis.

Physical examination is usually unremarkable in patients with coronary artery aneurysms; however, a mid-diastolic murmur may occasionally be heard.²³ Ring-calcification of the coronary arteries may be demonstrated on a chest radiograph.^{24,25} Capannari et al²⁶ reported a high sensitivity and specificity in detecting proximal aneurysms using two-dimensional echocardiography. Trans-esophageal echocardiography has also been useful in detecting coronary artery aneurysms.²⁷ However, coronary angiography is the diagnostic procedure of choice to visualize the entire coronary arterial system.

Symptoms of coronary artery aneurysms are usually the result of embolization of intraluminal thrombus into the distal tree, total occlusion of an involved artery, or slow or turbulent flow through the abnormal arteries. The symptoms include angina, congestive heart failure, and myocardial infarction. Sudden death and cardiac tamponade have been described in postmortem series.^{14,17,28-30} The association between coronary artery aneurysms and non-coronary artery aneurysms remains controversial. In Daoud et al's series,⁶ there was a high incidence of abdominal aortic aneurysms which were the most frequent cause of death. This association has not been confirmed by other workers.^{7,31,32}

The pathophysiologic process has been de-

TABLE I. Incidence of Coronary Artery Aneurysms in Published Angiographic Series

Published Series (ref)	No of Patients	No of CAA* (%)
CASS ¹	20,087	978 (4.9)
Hartnell ²	4,993	70 (1.4)
Aintablian ³	1,660	42 (2.5)
Swanton ⁴	1,000	12 (1.2)
Falsetti ⁷	742	11 (1.5)
Befeler ⁸	1,246	16 (1.3)
Markis ³¹	2,457	30 (1.2)
Oliveros ³²	1,000	5 (0.3)
Alford ⁴¹	1,654	37 (2.2)

*CAA = coronary artery aneurysms.

TABLE II. Distribution of the Coronary Artery Aneurysms

Published Series (ref)	Right Coronary Artery (%)	Left Circumflex Artery (%)	Left Anterior Descending Coronary Artery (%)
Hartnell ²	52/70 (40)	34/70 (24)	41/70 (29)
Aintablian ³	34/42 (53)	14/42 (22)	16/42 (25)
Daoud ⁶	8/10 (80)	2/10 (20)	2/10 (20)
Falsetti ⁷	23/34 (68)	23/34 (68)	17/34 (50)
Befeler ⁸	14/16 (87)	8/16 (50)	5/16 (31)
Oliveros ³²	7/11 (63)	6/11 (54)	6/11 (54)
Total	138/183 (75)	81/183 (44)	93/183 (51)

bated for many years. Aneurysms are of two types: saccular or fusiform. Saccular aneurysms are a globular outpouching of the arterial wall whereas fusiform aneurysms are an elongated cylindrical dilatation. Some workers suggest stenosis in a given vessel favors poststenotic dilatation.^{33,34} Befeler et al⁸ suggest other factors that may be operative in aneurysms formation, since fusiform aneurysms do not demonstrate narrowing. They suggest that primary changes in the media give rise to aneurysmal dilatation.

Markis et al³¹ reported that there is a high incidence of hypertension in patients with aneurysms and proposed that elevated blood pressure might play a role in the pathogenesis of the disease.

In several series, a high incidence of hypertension has been reported.^{6,8,31} However, in the CASS registry,¹ there was no significant difference between patients with aneurysmal or non-aneurysmal coronary artery disease with regard to incidence of hypertension, lipid profile, diabetes, family history, cigarette smoking, documented myocardial infarction, presence and severity of angina, and presence and severity of peripheral vascular disease. The five-year medical and surgical survival rate also showed no difference between patients with and without coronary artery aneurysms. Thus, coronary artery aneurysms do not appear to represent a separate clinical entity but rather a variant of coronary atherosclerosis.

The histological features of coronary artery aneurysms are diffuse hyalinization and lipid deposition with destruction of the intima and media. There is also focal calcification, fibrosis, and foreign body giant cell reaction. Once the media is involved, extensive destruction of the musculoelastic elements becomes apparent, resulting in a marked attenuation of the vessel wall.³¹

The clinical significance of coronary artery aneurysms continues to be debated. They predispose to angina, myocardial infarction, congestive heart failure, and sudden death,^{35,36} and some groups recommend surgery as the optimal treatment.³⁷⁻⁴² Ebert et al³⁸ first reported resection and bypass saphenous vein grafting in a 31-year-old patient. Anabtawi et al⁴² recommended bypass grafting only in proximal obstruction or saccular aneurysms. Glickel et al⁴⁰ suggested that resection was not indicated for small aneurysms or areas of ectasia associated with severe atherosclerotic disease.

These scattered cases of bypass graft surgery with or without resection are a subject of controversy. In the CASS registry,¹ the clinical outcome was the same for patients treated either medically or surgically regardless of the presence or absence of coronary artery aneurysms. Coronary artery aneurysms independent of coronary artery stenosis did not affect survival. However, management in these patient is still problematic, since the CASS data

do not represent a randomized trial but rather a report on the incidence of data in several subgroups. We should not apply conclusions based on these data to the general population.

The appropriate treatment of patients with coronary artery aneurysms is still not known. Nevertheless, prevention of thrombus formation appears logical. A trial of appropriate anticoagulant or antiplatelet therapy may be warranted in some patients.

REFERENCES

1. Swaye PS, Fisher LD, Litwin P, et al: Aneurysmal coronary artery disease. *Circulation* 1983; 67: 134-138.
2. Hartnell GG, Parnell BM, Pridie RB: Coronary artery ectasia: its prevalence and clinical significance in 4,993 patients. *Br Heart J* 1985; 54:392-395.
3. Aintablian A, Hamby RI, Hoffman I, et al: Coronary ectasia: incidence and results of coronary bypass surgery. *Am Heart J* 1978; 96:309-314.
4. Swanton RH, Thomas ML, Coltart DJ, et al: Coronary artery ectasia: a variant of occlusive coronary arteriosclerosis. *Br Heart J* 1978; 40:393-400.
5. Bougon A: *Biblioth Med* 1812; 37:183; as cited in Packard M, Wechsler H: Aneurysms of the coronary arteries. *Arch Intern Med* 1929; 43:1-14.
6. Daoud AS, Pankin D, Tulgan H, et al: Aneurysms of the coronary artery: report of ten cases and review of the literature. *Am J Cardiol* 1963; 11:228-236.
7. Falsetti HL, Carroll RJ: Coronary aneurysms: a review of the literature with a report of 11 new cases. *Chest* 1976; 69:630-636.
8. Befeler B, Aranda JM, Embi A, et al: Coronary artery aneurysms: study of their etiology, clinical course and effect on left ventricular function and prognosis. *Am J Med* 1977; 62:597-607.
9. Rath S, Har-Zahav Y, Battler A, et al: Fate of nonobstructive aneurysmal coronary artery disease: angiographic and clinical follow-up report. *Am Heart J* 1985; 109:785-791.
10. Gore T, Smith J, Clancy R: Congenital aneurysm of the coronary arteries with report of a case. *Circulation* 1959; 19:221-227.
11. Frithz G, Culhed T, Bjork L: Congenital localized coronary artery aneurysms without fistula. *Am Heart J* 1968; 76:674-679.
12. Rae MV: Coronary aneurysm with thrombosis in rheumatic carditis: unusual occurrence accompanied by hyperleukocytosis in a child. *Arch Pathol* 1937; 24:369.
13. Scott DH: Aneurysms of the coronary arteries. *Am Heart J* 1948; 36:403-413.
14. Schultz TC: Coronary artery aneurysms in a young adult. *Am J Forensic Med Pathol* 1989; 10:63-66.
15. Cullen S, Duff DF, Denham B, et al: Cardiovascular manifestations in Kawasaki disease. *J Med Sci* 1989; 158:253-256.
16. Konecke LL, Spitzer S, Mason D, et al: Traumatic aneurysm of the left coronary artery. *Am J Cardiol* 1971; 27:221-223.
17. Palmer P: Fatal ruptured mycotic coronary artery aneurysm. *P N G Med J* 1982; 25:281-282.
18. Whitehead R, Dunnell E: Primary dissecting aneurysms of coronary arteries. *J Pathol* 1969; 99:33-37.
19. Malloch JA: Dissecting aneurysms of coronary artery. *NZ Med J* 1974; 79:914-918.
20. Hill JA, Margolis JR, Feldman RL, et al: Coronary artery aneurysm formation after balloon angioplasty. *Am J Cardiol* 1983; 52:261-264.
21. Topaz O, DiSciascio G, Cowley MJ, et al: Angiographic features of left main coronary artery aneurysms. *Am J Cardiol* 1991; 67:1139-1142.
22. Tunick PA, Slater J, Kronzon I, et al: Discrete atherosclerotic coronary artery aneurysms: a study of 20 patients. *J Am Coll Cardiol* 1990; 15: 279-282.
23. Zoneraich S, Zoneraich O, Rhee JJ, et al: Giant coronary artery aneurysm: the cause of mid-diastolic murmur and bulging of the left cardiac border. *JAMA* 1975; 231:179.
24. Doi YL, Hamashige N, Odawara H, et al: Ring-calcification of coronary artery aneurysm in an adolescent. *Chest* 1987; 92:1118-1120.
25. Pearl WR, Kelly PC, Weir MR: Ring calcification of coronary artery aneurysms. *Chest* 1988; 94: 223-224.
26. Capannari TE, Daniels SR, Meyer RA, et al: Sensitivity, specificity and predictive value of two-dimensional echocardiography in detecting coronary artery aneurysms in patients with Kawasaki disease. *J Am Coll Cardiol* 1986; 7:355-360.
27. Tunick PA, Slater J, Pasternack P, et al: Coronary artery aneurysms: a transesophageal echocardiographic study. *Am Heart J* 1989; 118:176-179.
28. Cohle SD: Sudden unexpected death due to atherosclerotic coronary artery aneurysm. *Am J Forensic Med Pathol* 1985; 6:153-157.
29. Packard M, Wechsler H: Aneurysms of the coronary arteries. *Arch Intern Med* 1929; 43:1-14.
30. Trillo AA, Scharyj M, Prichard RW: Coronary artery aneurysm and myocardial infarction resulting in sudden death of a 6 year-old child: a case report. *Am J Forensic Med Pathol* 1980; 1:349-354.
31. Markis JE, Joffe CD, Cohn PF, et al: Clinical significance of coronary artery ectasia. *Am J Cardiol* 1976; 37:217-222.
32. Oliveros RA, Falsetti HL, Carroll RJ, et al: Atherosclerotic coronary aneurysms: report of 5 cases and review of literature. *Arch Intern Med* 1974; 134:1072-1076.
33. Holman E, Peniston W: Hydrodynamic factors in the production of aneurysms. *Am J Surg* 1955; 90:200-209.
34. Rodbard S, Ikeda K, Montes M: An analysis of the mechanisms of poststenosis dilatation. *Angiology* 1967; 18:349-367.
35. Jarvinen A, Pohjola-Sintonen S, Ketonen P, et al: Ruptured coronary artery aneurysm—a rare case of hemopericardium. *Thorac Cardiovasc Surg* 1985; 33:253-255.
36. Koike R, Oku T, Satoh H, et al: Right ventricular myocardial infarction and late cardiac tamponade due to right coronary artery aneurysm—a case report. *Jap J Surg* 1990; 20:463-467.
37. Gray LA, McMartin DE: Surgical treatment of coronary artery aneurysm with rupture to the right atrium. *J Thorac Cardiovasc Surg* 1977; 74:455-460.
38. Ebert PA, Peter RH, Gunnells JC, et al: Resecting and grafting of coronary artery aneurysm. *Circulation* 1971; 43:593-598.
39. Kitamura S, Kawashima Y, Miyamoto K, et al: Multiple coronary artery aneurysms resulting in myocardial infarction in a young man: treatment by double aorta-coronary saphenous vein bypass grafting. *J Thorac Cardiovasc Surg* 1975; 70:290-297.
40. Glickel SZ, Maggs PR, Ellis EH: Coronary artery aneurysms. *Ann Thorac Surg* 1978; 25:372-376.
41. Alford WC Jr, Stoney WS, Burrus GR, et al: Recognition and operative of patients with arteriosclerotic coronary artery aneurysms. *Ann Thorac Surg* 1976; 22:317-321.
42. Anabtawi IN, De Leon JA: Arteriosclerotic aneurysms of the coronary arteries. *J Thorac Cardiovasc Surg* 1974; 68:226-228.

Immunoglobulin-A plasma cell dyscrasia in a young Hispanic man

HANS W. GRUNWALD, MD; FRED ROSNER, MD; ANDREA C. KALMAN, RPA-C

Multiple myeloma is a neoplastic disease of plasma cells, which may invade bone marrow, cause skeletal (lytic) lesions, or present as single or multiple plasmacytomas. This disease occurs primarily in people over 50 years of age, but a small number of patients under the age of 30 have been described.¹⁻³ Younger patients, as a rule, tend to have a more indolent course than their older counterparts.² We report on a patient with immunoglobulin-A (IgA) multiple myeloma with two unusual features: age (25 years), and the aggressive nature of the disease.

CASE REPORT

A 25-year-old man presented in October 1987 with bilateral exophthalmos, generalized malaise, and weight loss. The patient had bilateral proptosis, lid lag, lid retraction, and upper lid edema. Fundoscopic examination showed papilledema on the right, and bilateral hemorrhages. Patient and family histories were non-contributory. He reported excessive alcohol consumption, but denied intravenous drug use. He stated that HIV testing had been negative.

Computed tomography scans of the head showed an enhancing mass in the middle cranial fossa bilaterally, extending laterally to the orbital wall on both sides and to the medial orbital wall on the left. There was also opacification of the frontal and sphenoid sinuses and left ethmoidal sinus.

The hemoglobin level was 6.7 g/dL; hematocrit was 18.7%; blood urea nitrogen was 52 mg/dL; creatinine was 6.5 mL/dL; total bilirubin was 1.7 mg/dL; calcium was 6.4 mg/dL; and uric acid was 14.8 µg/dL. The chest film showed bilateral pleural densities with pleural thickening, blunting of the costophrenic angles, and a bilateral diffuse reticulonodular infiltrative pattern with retrocardiac involvement. The bone marrow aspirate and biopsy contained 25% plasma cells and rare plasma blasts. Serum protein electrophoresis showed a spike in the gamma region with a broader downslope toward beta, suggesting polymers. Immunofixation revealed IgA-λ, with at least three areas of concentration suggesting

polymerization. The serum IgA level by immunonephelometry was 6,000 mg/dL. Serum viscosity was 5.5. Skeletal radiograph survey showed lytic lesions in the pelvis, proximal femur, and humerus. Pleural fluid was aspirated, and numerous plasmacytes were found. Urine electrophoresis revealed a prominent γ-spike.

The diagnosis of IgA multiple myeloma with retro-orbital plasmacytomas was made. The patient was treated with intravenous hydration for his renal failure, and the patient's phosphorus, uric acid, and calcium were all corrected with appropriate medications. The patient was transfused and given oral dexamethasone, 4 mg every 6 hr with significant reduction in proptosis within a few days.

Orbital irradiation and chemotherapy (oral alkeran) were then initiated. After a slow initial response to two courses, the patient thereafter received combination chemotherapy consisting of one dose of intravenous vincristine (2 mg), and oral melphalan (12 mg), cyclophosphamide (200 mg), and prednisone (100 mg), each for four days.⁴ He received five courses of this four drug regimen.

The IgA level decreased to 4,000 mg/dL, the hemoglobin improved to 13 gm/dL, and the ophthalmologic examination became normal. The chemotherapy was altered to intravenous cyclophosphamide, 1.7 g and oral prednisone, 40 mg daily for four days, every four weeks. The patient remained stable until April 1988, having received six courses of cyclophosphamide and prednisone, when the IgA level increased to over 9 g/dL, and the hemoglobin decreased to 9.7 g/dL. Chest radiograph indicated worsening of the pleural effusions and nodules, and the patient again became symptomatic in June 1988.

He was hospitalized for the last time in August 1988 for respiratory distress. *Staphylococcus aureus* was found in the blood, sputum and cerebral spinal fluid. Despite continued aggressive treatment, including antibiotics and dexamethasone, the patient expired in September 1988 from cardiopulmonary arrest secondary to myeloma, sepsis, bilateral pleural effusions, and renal failure. Autopsy was not performed.

DISCUSSION

Rapaport and Rowe² reviewed seven patients less than 30 years of age with plasma cell dyscrasias. Five of the seven had IgA paraproteins, and four had destructive bone lesions. The expected incidence of IgA myeloma is 28% as seen in Kyle's series of 869 cases of myeloma of all ages.⁵ The young patients in that review generally had indolent

courses and responded well to combination chemotherapy, with long-term responses.

Another reported case³ not included in the series by Rapaport et al was an 18-year-old woman with IgG myeloma who presented with orbital involvement with severe proptosis in addition to plasmacytomas of the sternum and clavicle. She had an excellent response to therapy. The investigators emphasize the rarity of orbital involvement in multiple myeloma (only a total of 33 cases reported through 1977).

The involvement of lung and pleura by plasma cell myeloma is also uncommon. A review of 958 myeloma patients seen at the Mayo Clinic,⁵ revealed radiographic abnormalities of the chest in 443, or 46%; nevertheless, in only 12 of these patients was the abnormality thought to be plasmacytic infiltration of lung and/or pleura, and it was documented in only nine patients (eight with myeloma cells in pleural effusion and one with plasmacytic pulmonary infiltrates). Although the plasmacytic nature of the nodular pulmonary infiltrates was only suspected in our patient, the myelomatous etiology of the pleural effusion was documented cytologically. Gurewal and Durie⁷ emphasize that pleuropulmonary myeloma is a rare manifestation of an aggressive type (or phase) of the disease.

The majority of young patients with myeloma have an indolent course and respond well to chemotherapy. Most of these patients, however, have IgA myeloma which usually has a shorter survival than IgG myeloma.⁸ Our patient had only a brief response to therapy and a short clinical course, probably because of his pleuro-pulmonary involvement, which carries a very ominous prognosis.

REFERENCES

1. Hewell GM, Alexanian R: Multiple myeloma in young persons. *Ann Intern Med* 1976; 84:441-443.
2. Rapaport AP, Rowe JM: Plasma cell dyscrasia in a 15-year-old boy: case report and review of the literature. *Am J Med* 1990; 89:816-818.
3. Levin SR, Spaulding AG, Wilman JA: Multiple myeloma: orbital involvement in a youth. *Arch Ophthalmol* 1977; 95:642-644.
4. Case DC, Lee BJ, Clarkson BD: Improved survival times in multiple myeloma treated with melphalan, prednisone, cyclophosphamide, vincristine and BCNU: M-2 protocol. *Am J Med* 1977; 63: 897-903.
5. Kyle RA: Multiple myeloma: review of 869 cases. *Mayo Clin Proc* 1975; 50:29-40.
6. Kintzer JS, Rosenow EC, Kyle RA: Thoracic and pulmonary abnormalities in multiple myeloma: a review of 958 cases. *Arch Int Med* 1978; 138:727-730.
7. Garewal H, Durie BGM: Aggressive phase of multiple myeloma with pulmonary plasma cell infiltrates. *JAMA* 1982; 248:1875-1876.
8. A Cooperative Study by Acute Leukemia Group B: Correlation of abnormal immunoglobulin with clinical features of myeloma. *Arch Int Med* 1975; 135:46-52.

From the Division of Hematology, Department of Medicine, Queens Hospital Center Affiliation of the Long Island Jewish Medical Center (Drs Grunwald, Rosner, and Kalman) and the Albert Einstein College of Medicine of Yeshiva University.

Address correspondence to Dr Rosner, Director, Department of Medicine, Queens Hospital Center Affiliation of the Long Island Jewish Medical Center, 8268 164th St, Jamaica, NY 11432.

Salmonella choleraesuis bacteremia and endocarditis in a patient with acquired immunodeficiency syndrome

DANIEL D. BUFF, MD; AKSHAY D. PATEL, MD; RICHARD B. NECHES, MD

The first cases of *Salmonella* infection in patients with the acquired immunodeficiency syndrome (AIDS) were reported in 1983.¹⁻⁵ It was subsequently estimated that 2% of AIDS patients are infected with *Salmonella*, a rate 20–100× that of the general population.^{6,7} It was also recognized that patients with AIDS are more likely to become bacteremic from a localized *Salmonella* infection.^{7,8} By 1987, recurrent *Salmonella* septicemia in a patient infected with the human immunodeficiency virus (HIV) was made a case definition for the diagnosis of AIDS.⁹

Most episodes of *Salmonella* bacteremia in HIV-positive patients are due to *S typhimurium*.^{7,8,10-12} To our knowledge, only two previous cases have been reported of AIDS patients bacteremic with *S choleraesuis*. Both of these patients were homosexual males with no reported history of intravenous drug abuse and no documented evidence of endocarditis.¹³ Three prior cases of *Salmonella* endocarditis in AIDS patients have been reported, one due to *S typhimurium*¹⁴ and two in which the subtype was not specified.^{1,15} We describe an HIV-positive heterosexual male with a history of intravenous drug abuse who developed *S choleraesuis* bacteremia and associated endocarditis.

CASE REPORT

A 46-year-old heterosexual male presented to the St John's Episcopal Hospital in September 1989 with a three-day history of fever, chills, and dry cough. The patient had been a chronic abuser of intravenous cocaine for six years and had ingested one pint of vodka per day for 12 years. His past medical history was significant for admission to another hospital in December 1985, with a diagnosis of *Salmonella* bacteremia and possible endocarditis (*Salmonella* subtype unknown). Two-dimensional echocardiograms at that time were normal, and he was not told he had a heart murmur. The patient was treated with six weeks of antibiotics and the only complication of treatment was the development of a diffuse body rash while on ampicillin. The patient

experienced no further infectious episodes until his current hospital admission. He was not previously tested for antibodies to the HIV virus.

On presentation, the patient complained of three days of fever to 103° F. The fever was associated with chills, generalized malaise, non-productive cough, mild headache, and pleuritic left sided chest pain. He denied anorexia, nausea, vomiting, abdominal pain, diarrhea, photophobia, or neck stiffness. Cocaine had been last injected five days before admission.

The initial physical examination revealed a toxic-appearing, well-developed white male with a normal blood pressure, a regular pulse of 86 b/min and a rectal temperature of 102° F. Extensive oropharyngeal candidiasis was noted. Kernig and Brudzinski signs were negative, the lungs were clear, and the cardiac examination was normal. The abdomen was non-tender and organomegaly was not present. There was no significant adenopathy and no peripheral manifestations of endocarditis were seen. Extensive needle track scars were noted on both upper extremities.

The admission white blood cell count was $6.0 \times 10^3/\text{L}$ (normal $4.8\text{--}10.8 \times 10^3/\text{L}$) with a differential of 86 segmented neutrophils, 3 band forms, and 11 lymphocytes. The hemoglobin was 13.5 g/dL (normal 14–18g/dL), and the platelet count was $52 \times 10^3/\text{L}$ (normal $130\text{--}400 \times 10^3/\text{L}$). Serum chemistries were normal except for a sodium of 121 mEq/L (normal 136–143 mEq/L) and an aspartate aminotransferase level of 52 U/L (normal 5–35 U/L). Both the chest x-ray and electrocardiogram were unremarkable.

The patient was admitted with presumptive diagnoses of septicemia and, given his history of drug use, possible endocarditis. After three sets of blood cultures were drawn, he was begun on empiric antibiotics with cephapirin 1-g IV Q8H and gentamicin 90-g IV leading dose followed by 60-g IV Q8H. A two-dimensional echocardiogram demonstrated a 5-mm vegetation on the tricuspid valve (Fig 1). The doppler examination was normal. On the third hospital day, two sets of blood cultures were reported growing *S choleraesuis*. Because the patient remained febrile and toxic, the antibiotics were changed to ceftriaxone at a dose of 1-g IV Q12H. The patient rapidly responded and completed a six week course of ceftriaxone. The only complication of treatment was a transient decline in the platelet count to $14 \times 10^3/\text{L}$. At no time did the patient develop diarrhea, and all stool cultures were negative for *Salmonella*. An ultrasound of the gallbladder re-



FIGURE 1. Two-dimensional echocardiogram, subcostal view (arrow indicates fixed lesion on the tricuspid valve consistent with a vegetation; RA = right atrium, RV = right ventricle).

vealed a solitary gallstone with no evidence of obstruction or inflammation. Testing for antibodies to HIV was positive by both enzyme-linked immunosorbent assay and Western blot techniques. A CD⁴ count was 142 lymphocytes/mm³.

During the fourth week of hospitalization, a one-to-two over six systolic murmur consistent with tricuspid regurgitation was noted. A second two-dimensional echocardiogram demonstrated that the tricuspid valve lesion was unchanged. The patient did not develop signs of right heart failure or embolization and the murmur remained unchanged. He was discharged on zidovudine (200 mg 5×/day) and trimethoprim-sulfamethoxazole (TMP-SMZ, one double-strength tablet twice a day and multivitamins). TMP-SMZ was continued for five months and the patient remained asymptomatic thereafter. Zidovudine was continued until June 1991, when the patient was lost to follow-up. No further echocardiograms were performed. There was no evidence of recurrent *Salmonella* infection, and there were no further hospitalizations.

DISCUSSION

The predisposition of AIDS patients for salmonellosis is primarily due to the impairment of cellular immune function by HIV infection. Because *Salmonella* organisms are intracellular pathogens, an intact T-cell-mediated response is necessary for adequate host defense.¹⁶⁻¹⁹ HIV infection impairs systemic T-cell function²⁰ and affects local responses in such tissues as the intestinal mucosa.²¹ This latter aspect is important as the

From the Department of Medicine (Drs Buff, Patel and Neches), St John's Episcopal Hospital, South Shore, Far Rockaway, NY.

Address correspondence to Dr Buff, Assistant Director, Department of Medicine, St John's Episcopal Hospital, 327 Beach 19th Street, Far Rockaway, NY 11691.

gastrointestinal tract is the portal of entry for most *Salmonella* species.¹⁶

Macrophage function is another component of cellular immunity that is compromised by HIV.²² Macrophages are directly infected by the virus and there is a decrease in T-cell production of macrophage stimulating factors.^{20,23,24} This combines to limit the ability of macrophages to control *Salmonella* infection. AIDS-related hemolysis may further reduce the macrophage response as erythrophagocytosis has been shown to interfere with the phagocytosis of *Salmonella* bacilli.^{8,25}

Predisposing factors other than deficient cellular immunity may also be important. Frequent use of antibiotics, which would be expected in immunodeficient patients, can alter normal intestinal flora. Competing organisms such as *Salmonella* are thereby able to flourish.¹⁸ Gastric acidity serves as an essential first line defense against ingested *Salmonella* bacilli,²⁵ and chronically ill AIDS patients may be more likely to experience achlorhydria.²⁶

As in the general population, the most frequent *Salmonella*-subtype associated with bacteremia in patients with AIDS is *S typhimurium*. A number of cases due to *S enteritidis* and *S dublin* have also been reported.^{7,8,10-12} To our knowledge, *S choleraesuis* bacteremia has previously been described in only two patients with AIDS, both homosexual males with no reported history of drug abuse and no diagnostic evidence of endocarditis.¹³ We found three published cases of *Salmonella* endocarditis in patients with AIDS, one due to *S typhimurium*¹⁴ and two in which the subtype was not specified.^{1,15}

S choleraesuis is considered to be the most invasive and virulent species of *Salmonella*.²⁵ Patients infected with *S choleraesuis* often become bacteremic and, of all *Salmonella* subtypes, this organism is associated with the highest proportion of fatal infections.²⁷ Despite being an infrequent isolate, *S choleraesuis* has been the most common *Salmonella* subtype to cause endocarditis.²⁵

Recommended therapy for salmonellosis in patients with AIDS has included ampicillin, chloramphenicol, and TMP-SMZ.^{16,18,28} Ampicillin is bactericidal for *Salmonella*, but its usefulness is limited by both the continuing emergence of ampicillin-resistant *Salmonella* strains²⁸⁻³⁰ and the high frequency of relapse.^{8,11,13,39} Chloramphenicol is not bactericidal for *Salmonella* and is associated with potentially life-threatening adverse reactions.²⁸ As many as 85% of patients with AIDS experience adverse reactions when treated with TMP-SMZ, many of these requiring discontinuation of the drug.^{31,32} These limitations have led to the search for alternative antibiotic regimens.

Favorable but limited experience has been reported with the third generation cephalosporin ceftriaxone and the quinolones ciprofloxacin and norfloxacin. Ceftriaxone is bactericidal for *Salmonella*, can be given intravenously once a day, and is well tolerated.²⁸ A recent letter described three AIDS patients with *Salmonella* gastroenteritis who responded well to ceftriaxone therapy.³³ Quinolones are particularly attractive as a potential treatment for *Salmonella* in patients with AIDS because of the potency of this class of drugs against *Salmonella* species, the low incidence of quinolone-associated adverse re-

actions, the ease of oral administration,²⁸ and the high intracellular concentrations obtained.³⁴ Ciprofloxacin has been employed with success in isolated AIDS patients^{35,36} as well as in a small group of AIDS patients with recurrent *Salmonella* bacteremia.³⁷ Norfloxacin has been efficacious in treating enteric salmonellosis in a series of nine patients with AIDS.³⁸ HIV-infected patients tend to suffer from persistent and recurrent *Salmonella* infections and long-term-suppressant therapy is generally recommended;^{8,19,39,40} quinolones appear well suited for this task.

Recently, the incidence of salmonellosis in AIDS patients appears to be declining.²⁶ Some feel that this is due to the antibacterial activity of the antiviral agent zidovudine.^{26,41,42} Zidovudine has been shown to have in-vitro activity against enterobacteriaceae, including *S typhimurium*.⁴³ Two French reports that studied the affect of zidovudine on salmonellosis in AIDS patients suggest that zidovudine may also have in-vivo activity against *Salmonella*. One study indicated that zidovudine may prevent an initial episode of *S bacteremia*⁴² and the second study indicated that zidovudine may prevent bacteremic relapse.⁴¹ The use of long-term TMP-SMZ treatment for prophylaxis against *Pneumocystis carinii* pneumonia may be another factor contributing to the apparent decline in the incidence of salmonellosis in HIV-positive patients.

In this report, we describe a heterosexual intravenous drug abuser who was seropositive for HIV infection and developed *S choleraesuis* septicemia. This was the patient's second episode of *Salmonella* bacteremia and, as such, we believe this patient meets established criteria for a diagnosis of AIDS. Although patients with AIDS appear to be at low risk for endocarditis (even those with a history of intravenous drug use),²⁴ we believe that the clinical and echocardiographic findings in our patient are consistent with a diagnosis of endocarditis due to *S choleraesuis*.⁴⁴ The patient had a normal echocardiogram with his prior episode of *Salmonella* septicemia; he had no episodes of endocarditis in the intervening period; and he now presented with positive blood cultures, a new tricuspid valve murmur, and a large vegetation on the tricuspid valve. It is true that a diagnosis of definite endocarditis cannot be made without a pathological specimen demonstrating such, but the patients' clinical presentation does allow for the diagnosis to be made with a high degree of probability.⁴⁵ Our patient responded well to six weeks of therapy with ceftriaxone. He received five months of suppressive therapy with TMP-SMZ and chronic treatment with zidovudine. This regimen evidently kept the patient free of recurrent *Salmonella* infection for a total follow-up period of 20 months.

As a treatable cause of infection, physicians should remain aware of the predisposition of AIDS patients for salmonellosis. Further research is needed to determine the optimal therapy for both acute and chronic *Salmonella* infection in this patient population.

Acknowledgments. The authors would like to thank Dr Kenneth Roistacher for his many helpful suggestions in the writing of this

paper, and Ms Kelly McGinn for her expert secretarial assistance.

REFERENCES

1. Pitchenik AE, Fischl MA, Dickinson GM, et al: Opportunistic infections and Kaposi's sarcoma among Haitians: evidence of a new acquired immunodeficiency state. *Ann Intern Med* 1983; 98:277-284.
2. Ammann AJ, Cowan MJ, Wara DW, et al: Acquired immunodeficiency in an infant: possible transmission by means of blood products. *Lancet* 1983; 1:956-958.
3. Clumeck N, Mascart-Lemone F, De-Maubeuge L, et al: Acquired immune-deficiency syndrome in black Africans (letter). *Lancet* 1983; 1:642.
4. Offenstadt G, Pinta P, Hericord P, et al: Multiple opportunistic infection due to AIDS in a previously healthy black woman from Zaire (letter). *N Engl J Med* 1983; 308:775.
5. Oleske J, Minnefor A, Cooper R Jr, et al: Immune deficiency syndrome in children. *JAMA* 1983; 249:2345-2349.
6. Profeta S, Forrester C, Eng RHK, et al: *Salmonella* infections in patients with acquired immunodeficiency syndrome. *Arch Intern Med* 1985; 145:670-702.
7. Celum CL, Chaisson RE, Rutherford GW, et al: Incidence of salmonellosis in patients with AIDS. *J Infect Dis* 1987; 156:998-1002.
8. Sperber SJ, Schleupner CJ: Salmonellosis during infection with human immunodeficiency virus. *Rev Infect Dis* 1987; 9:925-934.
9. Centers for Disease Control: Revision of the CDC surveillance case definition for acquired immunodeficiency syndrome. *MMWR* 1987; 36:1.
10. Glaser JB, Morton-Kute L, Berger SR, et al: Recurrent *Salmonella typhimurium* bacteremia associated with the acquired immunodeficiency syndrome. *Ann Intern Med* 1985; 102:189-193.
11. Nadelman RB, Mathur-Wagh U, Yancovitz SR, et al: *Salmonella* bacteremia associated with the acquired immunodeficiency syndrome (AIDS). *Arch Intern Med* 1985; 145:1968-1971.
12. De Wit S, Taelman H, Van de Perre P, et al: *Salmonella* bacteremia in African patients with human immunodeficiency virus infection. *Eur J Clin Microbiol Infect Dis* 1988; 7:45-47.
13. Fischl MA, Dickinson GM, Sinave C, et al: *Salmonella* bacteremia as manifestation of acquired immunodeficiency syndrome. *Arch Intern Med* 1986; 146:113-115.
14. Kinney EL, Monsuez JJ, Kitzis M, et al: Treatment of AIDS-associated heart disease. *Angiology* 1989; 40:970-976.
15. Bestetti RB, De Figueiredo JF, Da Costa JL: *Salmonella* tricuspid endocarditis in an intravenous drug abuser with human immunodeficiency virus infection. *Int J Cardiol* 1991; 30:361.
16. Hook EW: *Salmonella* species (including typhoid fever), in Mandell GL, Douglas RG Jr, Bennett JE (ed): *Principles and Practice of Infectious Diseases*, ed 3. New York, Churchill Livingstone, 1990, pp1700-1716.
17. Briles DE, Lehmeier J, Forman C: Phagocytosis and killing of *Salmonella typhimurium* by peritoneal exudate cells. *Infect Immun* 1981; 33:380-388.
18. Nencioni L, Villa L, Boraschi D, et al: Natural and antibody-dependent cell-mediated activity against *Salmonella typhimurium* by peripheral and intestinal lymphoid cells in mice. *J Immunol* 1983; 130:903-907.
19. Chaisson RE: Infections due to encapsulated bacteria, *Salmonella*, *Shigella*, and *Campylobacter*. *Infect Dis Clin North Am* 1988; 2:475-484.
20. Bowen DL, Lane HC, Fauci AS: Immunopathogenesis of the acquired immunodeficiency syndrome. *Ann Intern Med* 1985; 103:704-709.
21. Rogers VD, Kagnoff MF: Gastrointestinal manifestations of the acquired immune deficiency syndrome. *West J Med* 1987; 146:57-67.
22. Meltzer MS, Skillman DR, Gomatos PJ, et al: Role of mononuclear phagocytes in the pathogenesis of human immunodeficiency virus infection. *Ann Rev Immunol* 1990; 8:169-194.
23. Murray HW, Rubin BY, Masur H, et al: Impaired production of lymphokines and immune (gamma) interferon in the acquired immunodeficiency syndrome. *N Engl J Med* 1984; 310:883-889.

24. Cohen JI, Deresiewicz RL, Finberg RW: Fever, hypotension and pulmonary infiltrates in a young Haitian man. *Rev Infect Dis* 1988; 10:1052-1060.

25. Cohen JI, Bartlett JA, Corey GR: Extra-intestinal manifestations of *Salmonella* infections. *Medicine* 1987; 66:349-88.

26. Dellamonica P, Mondain V, Bernard E: Therapeutic aspects of salmonellosis in AIDS. *Pathol Biol* 1990; 38:298-301.

27. Rubin RH, Weinstein L: *Salmonellosis: Microbiologic, Pathologic and Clinical Features*. New York, Stratton Intercontinental Medical Book Corp, 1977.

28. Bryan JP, Rocha H, Scheld WM: Problems in salmonellosis: rationale for clinical trials with newer B-lactam agents and quinolones. *Rev Infect Dis* 1986; 8:189-207.

29. Cherubin CE: Antibiotic resistance to *Salmonella* in Europe and the United States. *Rev Infect Dis* 1981; 3:1105-1126.

30. Ryder RW, Blake PA, Murlin AC, et al: Increase in antibiotic resistance among isolates of *Salmonella* in the United States, 1967-1975. *J Infect Dis* 1980; 142:485-191.

31. Gordin FM, Simon GL, Wofsy CB, et al: Adverse reactions to trimethoprim-sulfamethoxa-

zole in patients with the acquired immunodeficiency syndrome. *Ann Intern Med* 1984; 100:495-499.

32. Glatt AE, Chirgwin K: *Pneumocystis carinii* pneumonia in human immunodeficiency virus infected patients. *Arch Intern Med* 1990; 150:271-279.

33. Rolston KVI, Rodriguez S, Mansell PWA: Antimicrobial therapy for *Salmonella* infections in the acquired immunodeficiency syndrome (AIDS) (letter). *Ann Intern Med* 1988; 108:309.

34. Andriole VT: Quinolones, in Mandell GL, Douglas RG, Bennett JE (ed.): *Principles and Practice of Infectious Diseases*. New York, Churchill Livingstone; 1990, 334-345.

35. Esposito S, Gaeta GB, Galante D, et al: Successful treatment with ciprofloxacin of *Salmonella typhimurium* infection in an immunocompromised host (letter). *Infection* 1985; 13:288.

36. Patton WN, Smith GM, Leyland MJ, et al: Multiply resistant *Salmonella typhimurium* septicemia in an immunocompromised patient successfully treated with ciprofloxacin. *J Antimicrob Chemother* 1985; 16:667-669.

37. Jacobson MA, Hahn SM, Gerberding JL, et al: Ciprofloxacin for *Salmonella* bacteremia in the acquired immunodeficiency syndrome (AIDS). *Ann Intern Med* 1989; 110:1027-1029.

38. Heseltine PN, Causy DM, Appleman MD,

et al: Norfloxacin in the eradication of enteric infections in AIDS patients. *Eur J Cancer Clin Oncol* 1988; 24:S25-28.

39. Jacobs JL, Gold JWM, Murray HW, et al: *Salmonella* infections in patients with the acquired immunodeficiency syndrome. *Ann Intern Med* 1985; 102:186-188.

40. Schrager LK: Bacterial infections in AIDS patients. *AIDS* 1988; 2:S183-188.

41. Salmon D, Detruichis P, Lepout C, et al: Efficacy of zidovudine in preventing relapses of *Salmonella* bacteremia in AIDS. *J Infect Dis* 1991; 163:415-416.

42. Dellamonica P, Bernard E, Pradier C, et al: AZT—does it prevent occurrence of salmonellosis in AIDS patients? *J Intern Med* 1991; 229:103.

43. Elwell LP, Ferone R, Freeman A, et al: Antibacterial activity and mechanism of action of 3'-azido-3'-deoxythymidine. *Antimicrob Agents Chemother* 1987; 31:274-280.

44. Smyllie JH, Sutherland GR, Roelandt J: The changing role of echocardiography in the diagnosis and management of infective endocarditis. *Int J Cardiol* 1989; 23:291-301.

45. Von Reyn CF, Levy BS, Abbeit RD, et al: Infective endocarditis: an analysis based on strict case definitions. *Ann Intern Med* 1981; 94:505-5518.

Health Fraud & Quackery



If it sounds too good to be true ...
it probably is.

HEALTH EDUCATION WEEK

NYS HEALTH DEPARTMENT

Address correspondence to Editor, New York State Journal of Medicine, 420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication after editorial review. All letters are personally acknowledged by the Editor.

A strong commitment to the New York State Journal of Medicine

TO THE EDITOR: I have heard that the Medical Society of the State of New York is considering changing the character of the *New York State Journal of Medicine* from a peer-reviewed scientific and clinical publication to one that would be more of an informal communication instrument. I recognize the financial pressures that play on an organization and understand that when that happens priorities need to be drawn up to decrease costs. I hope, however, you will make every effort to retain the *Journal*.

The history and tradition of medicine in New York State, although in some ways embattled, is a distinguished and proud one. It would be unfortunate, indeed, if our medical society could no longer publish a peer-reviewed journal so that it could take its place in the publications of medical societies and organizations. There is a strong commitment to the *Journal*, and, I believe, it has been strengthened and improved significantly in recent years. It should retain its place as an important means of clinical and scientific communication to the members of the Society. I do hope that in its careful scrutiny of activities that need to be reduced or eliminated the Society's leaders see fit to retain this most important activity and symbol of the leadership position and scientific contributions of physicians in the State of New York. We have a distinguished history in medicine and the *Journal* represents a tangible and important vehicle to represent that history and at the same time provide an important peer-reviewed current medical publication for the use of the Society's members.

MARSHALL A. LICHTMAN, MD
Dean, School of Medicine and Dentistry
University of Rochester Medical Center
601 Elmwood Avenue
Rochester, NY 14642

The fine national reputation of the New York State Journal of Medicine

TO THE EDITOR: I have heard a rumor that causes me considerable concern about the possibility of the *New York State Journal of Medicine* changing to a different format. I would be strongly opposed to such a course of action.

For many years, the *Journal* has served as a quality medical publication of peer-reviewed articles. The high standards set by the editor and the editorial board are a credit to the Society.

The reputation of the *Journal* extends far beyond the boundaries of New York State. In

my travels across the country, I frequently hear very fine comments about the *Journal*. I strongly support efforts to maintain it in its present format.

FRED ROSNER, MD
Assistant Dean and Professor of Medicine
Albert Einstein College of Medicine
Director
Department of Medicine
Long Island Jewish Affiliation at Queens
Hospital Center
82-68 164th Street
Jamaica, NY 11432

The importance of the New York State Journal of Medicine to the Medical Society

TO THE EDITOR: I am writing to urge the Medical Society of the State of New York to continue publication of the *New York State Journal of Medicine*. Many state journals have become just vehicles for state medical news and information. The *New York State Journal of Medicine* has a long and distinguished history of publishing useful and scholarly articles. It is recognized by a wide readership across the country.

There are many journals that could disappear without loss as they do not contribute new knowledge or high quality articles. The *New York State Journal of Medicine* is not one of them. Please continue this publication. Many of us feel it is one of the significant contributions of the Medical Society.

LUCRETIA M. CLURE
Medical Librarian
Edward G. Miner Library
University of Rochester Medical Center
601 Elmwood Avenue
Rochester, NY 14642

A suggestion for the New York State Journal of Medicine

TO THE EDITOR: We read with interest the article entitled "An update on the *New York State Journal of Medicine*" by Dr Gordon¹ and the correspondence by Dr Charatan.² We were surprised to learn that at present out of a total circulation of 27,595, only 0.6% of the subscriptions to this journal are foreign. To increase the number of foreign subscriptions, the *New York State Journal of Medicine* should actively encourage submissions of high-quality manuscripts from foreign authors. Foreign authors and their respective colleagues would be potential subscribers of the *Journal*.

ALEXANDER K. C. LEUNG, MBBS
WILLIAM LANE M. ROBSON, MD
SULAKHAN CHOPRA, BSC
University of Calgary
Alberta Children's Hospital
1820 Richmond Rd SW
Calgary, Alberta
Canada T2T 5C7

1. Gordon M: An update of the *New York State Journal of Medicine*. *NY State J Med* 1992; 92:294-296.
2. Charatan FB: The *New York State Journal of Medicine*. *NY State J Med* 1992; 92:408.

Foamy histiocytes and lepra bacilli in a lymph node aspirate

TO THE EDITOR: Hansen's disease (leprosy) is worldwide in its distribution. Skin and neuropathic lesions constitute the salient clinical features which can be quite protean in character. For those patients presenting with macular hypo-pigmented skin lesions, the differential diagnosis includes nevus anemicus, tinea versicolor, and vitiligo. For those patients presenting with papular, nodular, and plaque skin lesions, the differential diagnosis includes tinea corporis, pityriasis rosea, lymphoma cutis (mycosis fungoides), lichen planus, granuloma annularis, and sarcoidosis. For leprosy patients who present with polyneuropathy, the differential diagnosis includes chronic alcoholic intoxication, infection, the metabolic, autoimmune, and nutritional disorders, syringomyelia, and neurofibromatosis.

Fine-needle aspiration (FNA) is a simple, innocuous, and speedy technique which has become increasingly popular. This technique can provide a definitive diagnosis of leprosy.

Case Report. A 60-year-old black man was referred to the hematology out-patient clinic for evaluation of a macrocytic anemia and peripheral neuropathy. He was a native of Jamestown, Guyana who had immigrated to Brooklyn, New York in 1979. Shortly after his arrival, he was treated with antibiotics for cellulitis and osteomyelitis of his toes and right leg. About the same time, he complained of increasing numbness, tingling of both hands and feet, and of "things running over his face." A work-up for various muscular and neurological disorders, including a muscle biopsy was negative. A diagnosis of "sensory-neuropathy of stocking-glove distribution" type was proposed. Other differential diagnoses included arthritis and dermatitis. Several years later, he was found to have a hematocrit of 27% and was referred to the hematology clinic at this hospital for an evaluation of his anemia.

His history and physical examination were normal except for moderate night sweating and a mild fever (37.9° C). The presence of several palpable lymph nodes in his left axilla and along the great pectoral muscle was also noted. The most prominent lymph node measured approximately 1.5 cm. was soft, movable, mildly tender, and situated just beneath the skin and therefore easily accessible for a needle aspiration.

Laboratory study results were as follows: a hematocrit of 24%, hemoglobin 6.7 g/dL, white blood cell count of 9,800/mm³, with 72% neutrophils, 17% monocytes, 3% eosinophils, and 8% lymphocytes; the platelet count, 670,000/mm³. A bone-marrow aspirate was megaloblastic with an increased number of monocytic-macrophagic cells. Tests for measuring antibodies to human immunodeficiency virus (HIV) were negative. A culture for *Mycobacterium tuberculosis* as well as a PPD skin test were negative.

A no 21 needle attached to a 5 ml syringe was used to fill the needle with enough lymph node juices to make several smears on Baxter frosted and micro-glass-slides, which were stained with Wright's stain.

A Wright's stain of the FNA specimen revealed numerous foamy macrophages, both isolated and tightly packed sheets of cells characteristic of the morphology of lepra cells and clusters of lepra bacilli (Fig 1). Some of these organisms were extra-cellularly located, but most were found in the cytoplasm of histiocytes/macrophages. A biopsy of the same lymph node confirmed the findings and by using the Fite-Faraco staining (an acid fast stain) a much greater number of acid-fast lepra bacilli (*Mycobacterium leprae*) were found (Fig 2).

Discussion. Ridley and Jopling¹ divided leprosy into tuberculoid and lepromatous types as two polar forms with an intermediate, unstable, or borderline form in the middle of the spectrum.

The "indeterminate leprosy" described by Trautman² as the earliest stage, occurs after an incubation period of three to five years. This stage is characterized by the appearance of a few ill-defined-appearing asymptomatic, hypo-pigmented macules throughout the skin surface. This stage may resolve spontaneously

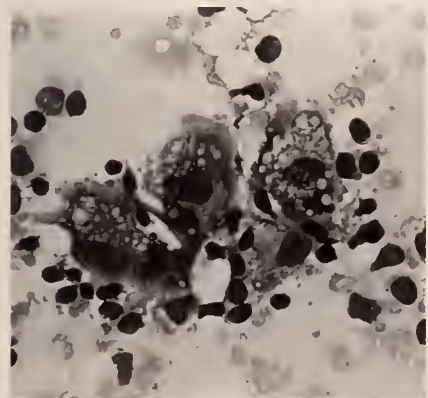


FIGURE 1. Large numbers of foamy histiocytes/macrophages (lepra cells) in lymph aspirate (Wright stain $\times 675$)

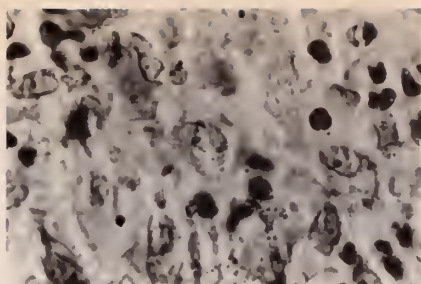


FIGURE 2. Large numbers of rod-like acid fast bacilli in the cytoplasm of the histiocytes/macrophages, lymph node (Fite-Faraco stain $\times 1,250$).

or progress to the intermediate (borderline), tuberculoid, or lepromatous phases.

The histological appearance of indeterminate hypo-pigmented skin lesions is that of non-specific chronic dermatitis. When the hypo-pigmented lesions are histologically characterized by dermal granulomas (containing few or no acid-fast bacilli) the patient has progressed to tuberculoid leprosy. This stage is characterized immunologically by patients mounting an adequate cell-mediated immune response which can be demonstrated in vivo by a lepromin test or by a standard intradermal skin test PPD.

The lepromatous phase is characterized by exhaustion of the cell mediated immune response by the host. The lesions of the lepromatous phase include macules, papules, plaques, and nodules. Nerve involvement produces autonomic and sensory dysfunction, motor disturbances, and atrophic changes in the skin. Histiocytes/macrophages laden with acid-fast bacilli are present in large numbers in the liver, spleen, bone marrow, testes, and lymph node.

The middle or intermediate spectrum consists of three variants: borderline tuberculoid, borderline borderline, and borderline lepromatous. These variants display a mixture of clinical, histopathological, and immunological features which is typical of tuberculoid and lepromatous leprosy (LL).

This case illustrates the presence of large numbers of acid-fast bacilli within histiocytes/macrophages in the lymph node with histopathological and immuno-pathological features of LL. The patient was treated with 100 mg dapsone daily and 600 mg rifampin weekly. Currently, the disease is in remission as judged by a disappearance of symptoms and enlarged lymph glands.

MICHAEL KHINE, MD
Department of Pathology
St Mary's Hospital
170 Buffalo Avenue
Brooklyn, NY 11213

1. Ridley DS, Jopling WH: Classification of leprosy according to immunity: a five-group system. *Int J Lepr Other Mycobact Dis* 1966; 34:255-273.

2. Trautman JR: Epidemiological aspects of Hansen's disease. *Bull NY Acad Med* 1984; 60:722-731.

3. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 49-1985. A 25-year-old Haitian man with Hansen's disease, painful subcutaneous nodules, fever, and hypesthesia. *N Engl J Med* 1985; 313:1464-1472.

The one white shirt

TO THE EDITOR: One of my favorite anecdotes has to do with a poor, young, college student who had basketball on his mind while his mother and her allies had other plans for him. Years after the event, he shared it with me in one of those reminiscing sessions that take place on a Sunday morning in the doctor's room.

With a rueful smile, he began by saying, "It was when I was a sophomore in college. I saved enough money to transfer to college in the daytime and was planning to spend my summer working and playing basketball. There were several moves I had been experimenting with, on my own. Now, they needed to be tried out in the school yard games. If they stood up there, the next step would be to use them in a real game situation."

"My day dreams took a bad bounce," he continued, "when my mother announced that our family physician and herself had been discussing my future. They decided that I should spend my summer as an observer in his hospital. Up to then, medicine was something we talked about, but not too seriously. When I pointed out the cost of all of this, she was adamant." Her parting statement was, "God will provide." I took my best shot and replied, "but I only have one white shirt, and I'll need a clean one everyday." Her response was to say nothing and to keep walking.

He paused, smiled, and went on. "She had it all worked out. Every day when I came from the hospital, I took off the shirt which she proceeded to wash and iron for the next day. This went on five days a week, all summer long. My sole thought was that next summer would be different."

"At the end of the summer she told me how pleased she was that every one at the hospital was so impressed with her son. They were so pleased, that they wanted me back next summer, and to that she had happily agreed."

Shaking his head and laughing, he went off to make rounds.

RANDALL D. BLOOMFIELD, MD
Associate Professor

Department of Obstetrics and Gynecology
State University of New York Health Science
Center at Brooklyn
450 Clarkson Avenue
Brooklyn, NY 11203

False-positive mammographic imaging of a breast implant

TO THE EDITOR: Mammography has long been used as the primary diagnostic imaging study for complications of breast augmentation. However, lack of accuracy of both mammographic information^{1,2} and clinical interpretation^{3,4} have necessitated the application of the non-x-ray modalities of light scanning, sonography, and duplex doppler ultrasound.

Case Report. A 40-year-old female had placement of a unilateral (right) breast implant for correction of breast asymmetry 17 years before her initial visit. She had sustained a Baker IV capsular contracture which led to the removal of the right implant and the

correction of the breast asymmetry by mastopexy and contralateral (left) breast reduction. Two months postoperatively a slowly enlarging right sided mass was noted. Mammograms were read as "silicone prosthesis in the right breast." A sonogram revealed a complex cystic structure (Fig 1). Transillumination showed marked light absorption characteristic of a hematoma. A duplex doppler sonogram demonstrated no flow patterns. At operation an organizing hematoma was found delimited by the implant capsule. The hematoma was evacuated and capsulectomy effected; the patient had an uneventful convalescence.

Discussion. Every plastic surgeon has received a radiologist's mammogram report on a patient with whom a long-standing implant has been removed for various complications, referring to the ovoid shaped density as a "prosthesis in position." Radiographically, a fibrous capsule cannot be differentiated from certain implant devices. In addition, a leakage of silicone gel that is restricted to the fibrous capsule is not separately distinguishable. Thus, x-rays are inadequate for the diagnosis of implant rupture except where the silicone has physically extruded through the capsule.^{5,6} Even then, the orthogonal routine views or the now popular anteroposterior and oblique positions may not demonstrate leakage that is close to the surface of the capsule. This leakage can only be identified by a tangential x-ray beam. An irregular outline of an implant may be positional, caused by adjacent breast pathology, resultant fibrous septation or actually due to implant rupture.

Sonographically, an implant is similar to a cyst. Thus, the size, shape, position, peripheral envelope, wall contour, and internal echo pattern are readily demonstrable. Rupture of an implant, whether from structural failure, intraoperative damage, penetrating trauma or blunt trauma such as closed capsulotomy, can be quickly and accurately diagnosed by routine high-frequency sonography.^{7,8}

Sonographic signs of implant rupture are linear echoes within the echo free area (this is distinguished from fibrous septation by the incomplete extent of the linear echo), gross

disruption of the capsule/envelope complex, and the presence of medium amplitude echoes floating within the fluid characteristic of clotted blood.

The role of light scanning is potentially important in the diagnosis of the etiology of the implant rupture. Although light scanning has been used for breast cancer detection and scrotal hydrocele analysis for many years, its usage in the augmented breast is relatively new while seemingly logical. Spontaneous failure of the envelope may be accompanied by fluid extravasation. If this process is localized, light scanning will be unremarkable.⁹ If the leakage is larger and more distant from the capsule, light absorption will be greater since the high light transmission by the implants silicone or water content is correspondingly lost in proportion to the spillage peripherally and compared with the unaffected normal contralateral side. It is important to realize that calcification does not affect the absorption of the optical transmission in the way that x-rays are absorbed by calcium. A long-standing leakage may become secondarily infected, this producing unilateral light absorption. Similarly, trauma, intraoperative or external, may be associated with bleeding that will also absorb light rays.¹⁰ Thus, a normal degree of transillumination may suggest that probability of structural intactness of the implant. Medium degrees of transmission blockage are associated with structural failure of the implant and massive light absorption loss accompanies hemorrhage and infection in the implant.

Duplex doppler is the combined application of high-resolution, real-time ultrasound and simultaneous doppler flow analysis (blood or other fluids) of the area under investigation. Therefore, duplex doppler may show linear fluid filled structures to be adjacent arteries or veins in contrast to centrally displaced prosthesis membrane.

Additionally, combined use of light scanning, sonography, and duplex doppler ultrasound, in addition to mammography (called multimodality breast imaging), may detect cancers, adjacent to and hidden by the implant.¹¹ Furthermore, the axillae may be imaged by the same ultrasound unit for the detection of lymphadenopathy as a result of breast carcinoma spread or secondary to accompanying inflammation of the breast or the capsule.¹²

ROBERT CUCIN, MD
ROBERT BARD, MD
120 Central Park South
New York, NY 10019

1. Smith DS: False-positive radiographic diagnosis of breast implant rupture: report of two cases. *Ann Plast Surg* 1985; 14:166-168.

2. Herzog P: Silicone granulomas detection by ultrasonography (letter). *Plast Reconstr Surg* 1989; 84:856-857.

3. Vogt PA, Seider HA, Moufarrege R: Surface-patterned silicone implants decrease contracture for soft breast prostheses. *Cont Surg* 1990; 37: 25-28.

4. Harper AP, Kelly-Fry E, Noe JS: Ultrasound in the evaluation of solid breast masses. *Radiology* 1983; 146:731-735.

5. Ho WC: Radiographic evidence of breast

implant rupture (letter). *Plast Reconstr Surg* 1987; 79:1,009-1,010.

6. Theophilis LG, Stevenson TR: Radiographic evidence of breast implant rupture. *Plast Reconstr Surg* 1986; 78:673-675.

7. Bard R, Hassani N: High resolution breast ultrasonography. *Diag Gyn Obstet* 1980; 2:303-312.

8. Levine RA, Collins RL: Definitive diagnosis of breast implant rupture by ultrasonography. *Plast Reconstr Surg* 1990; 87:1126-1128.

9. Adler D, Carson P, Rubin J: Doppler ultrasound color flow imaging in the study of breast cancer. *Ultrasound Med Biol* 1990; 16:553-559.

10. Gundersen J, Nilsson D, Ohlsson B: Diffraktion for bedomning av brostforandringar. *Lakartidningen* 1979; 76:1425-1426.

11. Britton P, Coulton R: The use of duplex doppler ultrasound in the diagnosis of breast cancer. *Clinical Radiology* 1990; 42:399-405.

12. Glynne-Jones R, Makepeace A, Spittle M: A possible role for ultrasound of the axilla in staging primary breast cancer. *Clin Oncol* 1990; 2: 35-39.

Gouty arthritis following gunshot wound

TO THE EDITOR: The article by Disla, Brar, and Taranta¹ requires correction. The injury which occurred to their patient and depicted in Figure 1 is not a gunshot wound, but a shotgun wound. Those caring for the acutely injured know that shotgun injuries are relatively uncommon, important, and fall within the broad spectrum of penetrating injuries due to firearms. Studies of ballistics and wounds emphasize the difference between single projectiles and shotgun injuries. In the latter, the variable wounding potential takes into account such factors as range, gauge of weapon, size of patter, and distance from victim to weapon.²

The ICD-9-CM codes separate the various mechanisms of external violence causing penetrating injuries. There are separate E-codes for shotgun injuries, as opposed to other types of shootings.

Although it may have no bearing on the described late sequelae of gouty arthritis, for the sake of wound care, epidemiology, and scientific accuracy, the distinction and correction should be noted.

DAN S. REINER, MD
Assistant Professor of Surgery
Cornell University Medical College
General Surgery
Chief, Division of Trauma/Surgical
Critical Care
North Shore University Hospital
300 Community Drive
Manhasset, NY 11030

1. Disla E, Brar H, Taranta A: Gouty arthritis following gunshot wound: a case report. *NY State J Med* 1992; 92:110-111.

2. Flint LM, Cryer HM, Howard DA, et al: Approaches to the management of shotgun injuries. *J Trauma* 1984; 24:415-419.

In reply. We appreciate Dr Reiner's comments about our article, "Gouty arthritis following gunshot wound: A case report."¹ We agree that our patient's injury was a shotgun wound. Nevertheless, even though



FIGURE 1. Duplex doppler. Echogenic complex cystic mass compatible with an organizing hematoma.

this is a more specific term, it also falls under the more general category of "gunshot," which refers to any "shot fired from a gun or just the firing of a gun," as defined in Webster's dictionary.²

Supporting this view, the *Index Medicus* has a heading only for gunshot wound but not for shotgun wound,³ this last term being considered a subtype of the first.

EDDYS DISLA, MD
Fellow, Rheumatology Service
Department of Medicine

ANGELO TARANTA, MD
Director, Department of Medicine
Cabrini Medical Center
277 East Nineteenth Street
New York, NY 10003

1. Disla E, Brar H, Taranta A: Gouty arthritis following gunshot wound: a case report. *NY State J Med* 1992; 92:110-111.

2. Webster's Ninth New Collegiate Dictionary, Springfield, Mass, *Cumulative Index Medicus*, vol 32, *Medical Subject Headings, Journals Indexed*, Bethesda, MD: National Library of Medicine, 1992 pp 220, 614.

Health Fraud Primer

What is health fraud? Health fraud is the promotion of useless or unproven remedies, for profit, usually by falsely representing that they will "cure" or aid in the cure of various diseases and problems.

Who are the victims of health fraud? Approximately 40 million Americans use fraudulent products each year. No one is immune. Its victims range from small infants to the elderly.

What are the costs of health fraud? Americans spend an estimated \$30 billion annually on worthless and often harmful products and treatments, but there are emotional and physical costs as well. One in every ten people who use fraudulent remedies is harmed by side effects. Others abandon legitimate treatments, often with tragic results.

What is a "quack"? A quack is a person who pretends to be able to cure a disease or health problem. Some quacks believe their own claims. A charlatan is a quack who knows his or her claim is false. Quacks tend to oversimplify, and pay more attention to the person's psychological need rather than the physical problem.

What are the most common forms of health fraud? According to the FDA, the most common forms of health fraud are fraudulent arthritis cures; spurious cancer clinics; bogus AIDS cures; instant weight-loss schemes; fraudulent sexual aids; quack appearance modifiers; and false nutritional schemes.

What is the best protection against health fraud? The best protection against health fraud is to become a well-informed and skeptical consumer of health products, devices and treatments.

How can a fraudulent claim be recognized? When considering an unknown product or service, look for these key phrases: "Quick and Easy Cure;" "Scientific Breakthrough;" "Natural Ingredients;" "Computerized Diagnosis;" and, "It Really Works!"

Who can help? If you think you've been taken in by a quack, contact the regional office of the US Food and Drug Administration, the US Postal Service (if the product was ordered or received by mail), the State Attorney General's office, the State Consumer Protection Board, or the State Health Department.

What is the most important thing to remember about health fraud? The most important thing to remember is: If it sounds too good to be true, it probably is!

Tarnished folk heroes in the battle against AIDS

Acceptable Risks. By Jonathan Kwitny. 466 pp. New York, Poseidon Press, 1992. \$24.95 (hardcover)

Jonathan Kwitny presents two tarnished folk heroes of the acquired immunodeficiency syndrome (AIDS) power revolution, Martin Delaney and Jim Corti, who with a network of associates accomplished three feats. The first was to help develop and accelerate the gray markets in anti-HIV drugs by buying illegally and selling to individuals and later to groups and buyers' clubs. The second was to pressure the Food and Drug Administration (FDA) to approve some drugs earlier than planned. The third was to force the FDA to compromise enforcement against their drug operations and renegade research projects.

The gray markets and drug underground accomplished little, except to allay fears and to instill a degree of hope. The second, shaking FDA's tree to allow expanded and accelerated access through legitimate channels was a plus, although it did not satisfy Delaney. The third, calling off enforcement against gray marketeers was either a con or a masterful piece of lobbying, or both. Kwitny pumps all three feats as major social advances. In the world according to Kwitny, his protagonists are freedom fighters, and the antagonists are egotistical bureaucratic dysfunctionaries.

The book jacket states, "The explosive politics of life vs profit in America—how two courageous men fought the FDA to save thousands of AIDS patients, and changed the drug industry forever." If this sounds like puffery, it nevertheless reverberates throughout the book. The facts are that most of the drugs the heroes supplied are ineffective. None has cured AIDS, few have prolonged life, and those were already near approval. Even prophylactic aerosolized pentamidine, over which Kwitny and Delaney fussed, was rapidly supplanted by safer and cheaper drugs.

Kwitny is a reporter whose previous works explore intrigue and conspiracies, CIA and the drug trade, and the like. *Acceptable Risks*, comes off as a morality play—an unlikely contest of heroes and villains, undercover operations, games of wit and outwit, politics and economic self-interest, on the tragic background of AIDS and the gay community. Delaney and Corti are the "good guys" and FDA and responsible medical researchers are "bad guys" (terms used in this book).

"*Risks*" describes several episodes in Delaney's and Corti's association. They first crossed while both ran contraband ribavirin from Mexican pharmacies to United States buyers,

making end runs around border inspectors and airport customs agents. Their next foray was shipping loads of low molecular weight dextran from Japan to the United States, with Corti again outwitting both Japanese authorities and US Customs. The last two Delaney projects were the renegade compound Q study and the underground sale of DDC. In these, we see Delaney as master lobbyist, power broker, and manipulator of officials.

There are meetings with former FDA Commissioner Frank Young, C. Boyden Gray (then VP Bush's closest advisor), and cross-country telephone calls with researchers Robert Gallo and Anthony Fauci. No question that everyone in the AIDS scene knows Martin Delaney.

Among others given bad press is Ellen Cooper, MD, of the FDA for attempting to assure proof of safety and effectiveness before approval of drugs. The principle is challenged by Delaney. In answer to the criticism that uncontrolled drug availability would ruin research projects (subjects in drug research must adhere to the protocol and not cheat on what they take,) Delaney claims that if experimental drugs were freely available, research projects would attract the more reliable volunteers. Who but Delaney, Kwitny, and friends could believe that?

Derision of the bad guys extends to their clothing. FDA's Frank Young has a penchant for white Public Health Service Uniforms. Donald Abrams of the San Francisco AIDS Consortium and the San Francisco General AIDS research team is fond of striped shirts, large paisley bow ties, and running shoes, but Martin Delaney wears a conservative dark gray business suit and striped tie. The book raises such irrelevancies to high political significance.

The book does not record lives saved or even days lived longer through the efforts of its heroes, but we are left a legacy of unequal enforcement of the law with which we will all have to deal later.

WALLACE I. SAMPSON, MD

Clinical Professor of Medicine
Stanford University School of Medicine
Acting Chief, Oncology Division
Santa Clara Valley Medical Center
751 South Bascom Ave
San Jose, CA 95128

Classified Advertising

PRACTICES AVAILABLE

PRACTICES FOR SALE: 1) Family Practice/Accupuncture, Ulster County, N.Y.; 2) Pediatrics—Central New Jersey, retiring; 3) Ophthalmology—Northern New Jersey, part-time; Contact: Epstein Practice Brokerage, Inc. (212) 233-7300.

BEVERLY HILLS AREA—Dermatology Practice available for purchase. Close to Beverly Hills, practice is well established. Practitioner has excellent reputation. Doctor will assist in transition. Reason for sale, physician desires to relocate. Please send inquiry to: Box A, 1445 S. Cardiff Avenue, Los Angeles, CA 90035.

LOS ANGELES—Fully equipped building with x-ray, physical therapy, EKG, treadmill, spirometer. Building for sale. Practice focuses on Ethical Medical Evaluation of Chemical Exposure, some General Practice as well. Practitioner has excellent reputation. He will assist in transition. Please send inquiry to: Box B, 1445 S. Cardiff Avenue, Los Angeles, CA 90035. Reason for sale, physician desires to relocate.

MARVELOUS OPPORTUNITY for Board Certified/Board Eligible Cardiologist looking to relocate, expand or purchase existing practice in Mid-Hudson Valley Region, New York. 7½ year old practice with 2,000 plus active patients in a new contemporary office building. Office is completely and beautifully furnished and is equipped with state of the art medical equipment. Doctor is relocating out of state on or about June 1, 1993. For additional information, please contact: Mary Ann Hamburger at 201-763-7394.

REAL ESTATE FOR SALE OR RENT

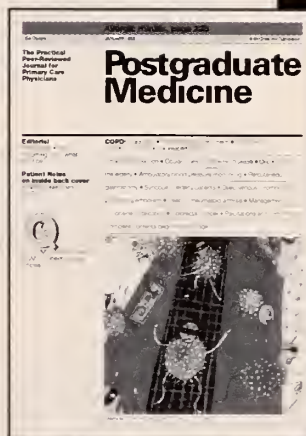
MANHATTAN'S UPPER EAST SIDE, 133 EAST 73 STREET. Lexington Professional Center. Hourly, part-time or full-time medical and psychiatric suites. Fully furnished and equipped. 24-hours answering service, receptionist, and mail service. Clinical laboratory on premises. No leases required, no minimum hours required. (212) 861-9000.

FOR SALE: EAST SIXTIES, PROFESSIONAL BUILDING. Large medical office (2,250 sq. ft.). 3 consultation rooms, 4 treatment rooms, laboratory, 2 bathrooms, large reception area. Also suitable for dentist. Full-time doorman. Call (212) 838-2860.

SHARE OFFICE Most Prestigious Location near St. Barnabas Medical Center, Livingston, N.J., Telephone Arthur Winter, M.D., (201-992-3300).

WEST HEMPSTEAD BORDERING GARDEN CITY (N.Y.) Professional suite + Residence + Mother/Daughter basement apartment. 4 bedrooms, 4 bathrooms, 3 floors, all new designer kitchen, 2 car garage, charming Tudor. Principals only. \$299,000.00 Tel # 516-538-2761.

US THEM



Postgraduate Medicine

WHEN YOU NEED TIME ON YOUR SIDE, THE CHOICE IS CLEAR.

NO CLINICAL CLUTTER—PGM ARTICLES ARE CLEAR, CONCISE, WELL ILLUSTRATED, AND PRACTICAL.



Since St. Jude Children's Research Hospital opened in 1962, it has forged new treatments for childhood cancer and has helped save the lives of thousands of children around the world. But the battle has just begun. You can join the fight. To find out how, call 1-800-877-5833.



**ST. JUDE CHILDREN'S
RESEARCH HOSPITAL**

Danny Thomas, Founder

REAL ESTATE FOR SALE OR RENT—CONT'D

OUTSTANDING HOME/OFFICE — Corner location. For full or part time practice in prestigious North Syosset, L.I. 8 rooms, 3 bath ranch, oversized garage, I.G.P., fireplace, oak floors, pine panelled basement, alarm systems plus three room office, ½ bath, 2 separate entrances. Walking distance to outstanding school and railroad. Low \$300's. Telephone (516) 921-3645.

MISCELLANEOUS

PROFESSIONAL CONDUCT EXPERT. Robert S. Asher, J.D., M.P.A., in health, former Director Professional Conduct, N.Y.S. Board of Regents, now in private legal practice. 15 years health law experience concentrating on professional practice, representation before government agencies on Disciplinary, Licensure, Narcotic Control, Medicaid, Medicare of Third-Party Reimbursement matters and professional business practice. Robert S. Asher, Esq., 295 Madison Ave., Suite 700, NYC. (212) 697-2950 or evenings (914) 723-0799.

SONOGRAMS—Cardiac echo, osteoporosis bone densitometry. In your office or patient's home. Legally proper rent arrangements. 718-367-7667.

MISCELLANEOUS—CONT'D

IS ACTION BEING TAKEN AGAINST YOUR LICENSE TO PRACTICE MEDICINE? If affirmative, contact Susan Kaplan, Attorney-at-Law, (212) 877-5998. Practice limited to assisting, advising and defending physicians in professional misconduct (licensure) proceedings before the Office of Professional Medical Conduct, issues relating to chemical dependence and restoration of medical licenses—with extensive trial and administrative experience—formerly Assistant Chief of Prosecution and Deputy Director of Prosecution for New York State's Office of Professional Discipline (the state agency responsible for regulating NYS's 31 licensed professions), and as an Assistant District Attorney in Nassau County.

MEDICAL TRANSCRIPTION—Nassau County. 25 Years' experience. Thorough knowledge of all medical specialties. IBM Wordprocessing, Microbank-25, Modern transmittal available. Phone in dictation. Patient chart notes, in-office tests, consultation letters. Call Wordbusters (516) 333-8660.

WOOD & SCHER, ATTORNEYS AT LAW. Former Chief Enforcement Officers for the Office of Professional Discipline, now representing licensed professionals in matters of: Professional misconduct proceedings, License application/restoration, Controlled Drug Proceedings, Medicaid/Medicare Proceedings, Hospital Privileges, Malpractice Defense. Call for a consultation William L. Wood, Jr. and Anthony Z. Scher, (914) SCarsdale 3-3500.

PHYSICIANS SIGNATURE LOANS TO \$50,000. Take up to 7 years to repay with no pre-payment penalties. Competitive fixed rate. Use for taxes, investment consolidation or any other purpose. Prompt, courteous service. Physicians Service Association, Atlanta, GA. Serving MD's for over 10 years. Toll-free (800) 241-6905.

WANT DISCOUNTS ON YOUR EXISTING INSURANCE? We provide complimentary 2nd opinions on your disability and life insurance to provide you with the lowest rates. Servicing physicians exclusively. References provided upon request. Paul R. Sheinkopf, Sheinkopf & Associates, EAB Plaza West, 5th floor, Uniondale, NY 11556-0137. 516-357-8700 FAX 516-357-8891.

HIGH QUALITY TRANSCRIPTION at an affordable price. All specialties. Also medicolegal transcription, journal articles, manuscripts and book chapters expertly done. Audiocassettes, on-line phone dictation 24-hours per day 7 days per week. Competitive prices. Call 718-225-0806.

REPRESENTATION OF PHYSICIANS and advice and counsel with respect to licensure and professional conduct matters, audit preparations, reimbursement issues and governmental inquiries and investigations. David E. Ruck, Esq., former Chief, Criminal Division, Office of the New York State Special Prosecutor for Medicaid Fraud Control. Mr. Ruck's law offices: 230 Park Avenue, Suite 2830, New York, New York 10169. Telephone 212-661-8070.

MISCELLANEOUS—CONT'D

SHAPIRO & BYRNE, P.C., ATTORNEYS AT LAW. Daniel M. Shapiro, M.D., J.D. Professional misconduct representation including disciplinary proceedings, medical staff problems and hospital privileges, peer review proceedings and other matters affecting the professional life of physicians. 220 Old Country Road, Mineola, N.Y. (212) 514-5755, (516) 877-1055.

PROFESSIONAL MISCONDUCT ADVOCACY with dignity and concern. George Weinbaum, Esq., former deputy director of the New York State Attorney General's office for Medicaid Fraud Control and also former Director of Medicare and private insurance investigations for Empire Blue Cross/Blue Shield. Extensive experience and attention is devoted to Misconduct Avoidance, Disciplinary Proceedings, Medicaid/Medicare issues, Controlled Drug Proceedings, Audits, and Federal/State civil and criminal investigations. Consultations available. George Weinbaum, Esq., 3 Barker Avenue, White Plains, New York 10601. Telephone (914) 686-9310—24 hours.

LIFSHUTZ, POLLAND & ASSOCIATES, P.C. The law firm that specializes in health care representation. Our experienced staff of attorneys have successfully represented physicians and other health care professionals in such matters as managed care ventures and contracts, establishment of medical groups, counseling professional societies and hospital medical staffs, hospital privileges, defense of Medicaid/Medicare abuse allegations (civil and criminal), third-party beneficiary termination, peer review, challenging legislative and regulatory enactments, leasing and subleasing of medical office space, tax and pension plan structuring of professional corporations, estate planning, litigation of rights and interests of clients including equitable distribution of physician's licenses in matrimonial actions. Lifshutz, Polland & Associates, P.C., Attorneys at Law, 675 Third Avenue, New York, N.Y. 10017. (212) 949-8484.

Index to Advertisers

Bristol Myers	3rd & 4th Cover
Classified	8A, 9A, 10A
CompHealth	8A
Comprehensive Headache Center	3A
Hospital Underwriters Mutual	1A
Eli Lilly and Company	2nd Cover
McGraw Hill Publications	9A
MLMIC	7A
Palisades Pharmaceuticals	5A
U.S. Air Force	8A

PRAVACHOL® (Pravastatin Sodium Tablets) CONTRAINDICATIONS

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

Pregnancy and lactation. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of child-bearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

WARNINGS

Liver Enzymes: HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in ALT and AST equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected. Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.**

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when diltiazem was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when diltiazem therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

PRECAUTIONS

General: Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

Homozygous Familial Hypercholesterolemia. Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

Renal Insufficiency. A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 α -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life ($t_{1/2}$) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

Information for Patients: Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

Drug Interactions: Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin: See WARNINGS. Skeletal Muscle.

Antipyrene: Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

Cholestyramine/Colestipol: Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

Warfarin: In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C_{max} of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

Cimetidine: The AUC_{0-12h} for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

Digoxin: In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

Gemfibrozil: In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C_{max}, and T_{max} for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids (1 hour prior to PRAVACHOL), cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL (pravastatin sodium) was administered.

Other Drugs: During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

Endocrine Function: HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced ($p < 0.004$) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a $\geq 50\%$ rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin should display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

CNS Toxicity: CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class was produced in optic degeneration (Kallman's degeneration of retinogeniculate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear (Wallerian-like) degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose ($p < 0.01$). Although rats were given up to 125 times the human dose (H-D) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls ($p < 0.05$). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (at total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*; a forward mutation assay in L5178Y TK +/– mouse lymphoma cells; a chromosomal aberration test in hamster cells; and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

Pregnancy: Pregnancy Category X: See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/meter²). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL (pravastatin sodium), it should be discontinued and the patient advised again as to the potential hazards to the fetus.

Nursing Mothers: A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

Pediatric Use: Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

ADVERSE REACTIONS

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy; this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

Adverse Clinical Events: All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug.

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

Skeletal: myopathy, rhabdomyolysis.

Neurological: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

Gastrointestinal: pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

Reproductive: gynecomastia, loss of libido, erectile dysfunction.

Eye: progression of cataracts (lens opacities), ophthalmoplegia.

Laboratory Test Abnormalities: Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, Thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

Concomitant Therapy: Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is **not** associated with greater reduction in LDL-cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended. (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

OVERDOSAGE

There have been no reports of overdoses with pravastatin.

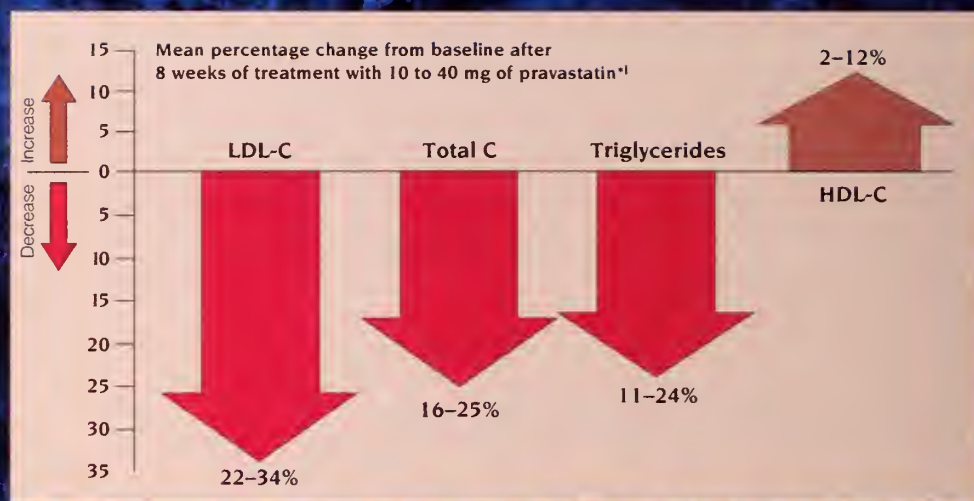
Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.





Effective cholesterol control

Consistently and significantly reduces total C and atherogenic LDL-C; positively affects other key lipids



*Each arrow represents a range of means derived from a single placebo-controlled study that included 55 patients treated with pravastatin.

PRAVACHOL[®] (pravastatin sodium) is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate.

Active liver disease *or* unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin.

Reference: 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol.* 1991;14:146-151.

PRAVACHOL[™]
pravastatin sodium 20 mg tablets

Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



Bristol-Myers Squibb Company

New York State Journal of Medicine



VOL 93
NO 3
MARCH
1993

**ISCHEMIC STROKE IS
PREDICTABLE AND
PREVENTABLE**

**SOFT TISSUE
SARCOMAS—IS ADJUVANT
CHEMOTHERAPY
INDICATED?**

**PERSONAL AND
SELF-DIRECTED CONTINUING
MEDICAL EDUCATION**

**WHEN DEATH RESTORES
LIFE**

**QUALITY OF CARE
PROBLEMS AMONG
MEDICARE PATIENTS IN
NYS**

**PERIOPERATIVE STROKE
AFTER GENERAL SURGICAL
PROCEDURES**

**COMPLIANCE WITH NYS's
DNR LAW AT MEMORIAL
SLOAN-KETTERING CANCER
CENTER**

PROTECTING YOUR PRACTICE IS A SIMPLE PROCEDURE WHEN YOU USE THE RIGHT INSTRUMENT.



Outstanding professional liability coverage and superior service are just a phone call away—with HUM.

To make your practice as safe as it can be, you need more than just insurance. You need a well-managed program to reduce risk. Education to keep current on important issues. Consultants to suggest alternatives—and work *with* you to implement them. You need to connect with HUM.

Every policy is based on partnership.

When HUM writes you a policy, we make a real commitment to serving you—from designing cost-effective coverage, to enhancing your risk management efforts, to managing claims prudently and professionally.

Along with unmatched financial strength, we offer competitive premiums, discounts for first-year and part-time practitioners, plus a range of flexible payment plans.

Best of all, it's simple to put our advantages into practice. Just dial 1-800-435-3558 for more information about HUM's policies.

We're on call for physicians.

A policy of partnership.



Hospital Underwriters Mutual
Insurance Company

FREEDOM FROM PAIN!

**Extra strength pain relief
free of extra prescribing
restrictions.**

- Telephone prescribing in most states
- Up to five refills in 6 months
- No triplicate Rx required

**15 years of proven
clinical experience**

- Effective central and peripheral pain relief.
- Excellent patient acceptance—nausea, sedation and constipation have rarely been reported.¹
- Four to six hours of extra strength pain relief from a single dose.
- The heritage of VICODIN[®] — over one billion doses prescribed.²
- The 8th most frequently prescribed medication in America.²

vicodin ES 

(hydrocodone bitartrate 7.5mg [Warning: May be habit forming]
and acetaminophen 750mg)

**Extra strength pain relief
you can phone in.**

¹ Data on file, Knoll Pharmaceutical Company

² Standard industry new prescription audit.

* (hydrocodone bitartrate 5mg [Warning: May be habit forming] and acetaminophen 500 mg)



Maintain control of your patient's pain therapy.

R_x
Specify
*Do not
substitute*

vicodin ES 

(hydrocodone bitartrate 7.5mg (Warning: May be habit forming)
and acetaminophen 750mg)

It's your prescription – not a suggestion.

INDICATIONS AND USAGE: For the relief of moderate to moderately severe pain. **CONTRAINDICATIONS:** Hypersensitivity to acetaminophen or hydrocodone. **WARNINGS: Respiratory Depression:** At high doses or in sensitive patients, hydrocodone may produce dose-related respiratory depression. **Head Injury and Increased Intracranial Pressure:** The respiratory depressant effects of narcotics and their capacity to elevate cerebrospinal fluid pressure may be markedly exaggerated in the presence of head injury, other intracranial lesions or a preexisting increase in intracranial pressure. Furthermore, narcotics produce adverse reactions which may obscure the clinical course of patients with head injuries. **Acute Abdominal Conditions:** The administration of narcotics may obscure the diagnosis or clinical course of patients with acute abdominal conditions. **PRECAUTIONS: Special Risk Patients:** VICODIN/VICODIN ES Tablets should be used with caution in elderly or debilitated patients and those with severe impairment of hepatic or renal function, hypothyroidism, Addison's disease, prostatic hypertrophy or urethral stricture. **Cough Reflex:** Hydrocodone suppresses the cough reflex; as with all narcotics, caution should be exercised when VICODIN/VICODIN ES Tablets are used postoperatively and in patients with pulmonary disease. **Drug Interactions:** Patients receiving other narcotic analgesics, antipsychotics, anti-anxiety agents, or other CNS depressants (including alcohol) concomitantly with VICODIN/VICODIN ES Tablets may exhibit an additive CNS depression. The use of MAO inhibitors or tricyclic antidepressants with hydrocodone preparations may increase the effect of either the antidepressant or hydrocodone. The concurrent use of anticholinergics with hydrocodone may produce paralytic ileus. **Use in Pregnancy: Teratogenic Effects:** Pregnancy Category C. Hydrocodone has been shown to be teratogenic in hamsters when given in doses 700 times the human dose. There are no adequate and well-controlled studies in pregnant women. VICODIN/VICODIN ES Tablets should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. **Nonteratogenic effects:** Babies born to mothers who have been taking opioids regularly prior to delivery will be physically dependent. The withdrawal signs include irritability and excessive crying, tremors, hyperactive reflexes, increased respiratory rate, increased stools, sneezing, yawning, vomiting, and fever. **Labor and Delivery:** Administration of VICODIN/VICODIN ES Tablets to the mother shortly before delivery may result in some degree of respiratory depression in the newborn, especially if higher doses are used. **Nursing Mothers:** It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from VICODIN/VICODIN ES Tablets, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother. **Pediatric Use:** Safety and effectiveness in children have not been established. **ADVERSE REACTIONS:** The most frequently observed adverse reactions include light-headedness, dizziness, sedation, nausea and vomiting. These effects seem to be more prominent in ambulatory than in nonambulatory patients and some of these adverse reactions may be alleviated if the patient lies down. Other adverse reactions include: **Central Nervous System:** Drowsiness, mental clouding, lethargy, impairment of mental and physical performance, anxiety, fear, dysphoria, psychic dependence and mood changes. **Gastrointestinal System:** The antiemetic phenothiazines are useful in suppressing the nausea and vomiting which may occur (see above); however, some phenothiazine derivatives seem to be antianalgesic and to increase the amount of narcotic required to produce pain relief, while other phenothiazines reduce the amount of narcotic required to produce a given level of analgesia. Prolonged administration of VICODIN/VICODIN ES Tablets may produce constipation. **Genitourinary System:** Urteral spasm, spasm of vesical sphincters and urinary retention have been reported. **Respiratory Depression:** Hydrocodone bitartrate may produce dose-related respiratory depression by acting directly on the brain stem respiratory center. Hydrocodone also affects the center that controls respiratory rhythm, and may produce irregular and periodic breathing. If significant respiratory depression occurs, it may be antagonized by the use of naloxone hydrochloride. Apply other supportive measures when indicated. **DRUG ABUSE AND DEPENDENCE:** VICODIN/VICODIN ES Tablets are subject to the Federal Controlled Substance Act (Schedule III). Psychic dependence, physical dependence, and tolerance may develop upon repeated administration of narcotics; therefore, VICODIN/VICODIN ES Tablets should be prescribed and administered with caution. **OVERDOSAGE: Acetaminophen Signs and Symptoms:** In acute acetaminophen overdosage, dose-dependent, potentially fatal hepatic necrosis is the most serious adverse effect. Renal tubular necrosis, hypoglycemic coma, and thrombocytopenia may also occur. Early symptoms following a potentially hepatotoxic overdose may include: nausea, vomiting, diaphoresis and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion. **Hydrocodone Signs and Symptoms:** Serious overdose with hydrocodone is characterized by respiratory depression (a decrease in respiratory rate and/or tidal volume, Cheyne-Stokes respiration, cyanosis), extreme somnolence progressing to stupor or coma, skeletal muscle flaccidity, cold and clammy skin, and sometimes bradycardia and hypotension. In severe overdosage, apnea, circulatory collapse, cardiac arrest and death may occur.

Revised March 1992

5890

Knoll Pharmaceutical Company
30 North Jefferson Road
Whippany, New Jersey 07981

BASF Group



New York State Journal of Medicine



COMMITTEE ON PUBLICATIONS, LIBRARY, AND ARCHIVES

MILTON GORDON, MD, Chairman

PHILIP P. BONANNI, MD, Vice-Chairman

JOSEPH I. COHN, MD
JONATHAN A. HYDE (Medical student)
STANLEY LUFTSCHEIN, MD
SHARON C. HERMAN MEAD, MD
JOSEPH F. MURATORE, MD
DONNA B. O'HARE, MD
JOHN T. PRIOR, MD

Editor PASCAL JAMES IMPERATO, MD
Consulting Editor JOHN T. FLYNN, MD
Consulting and Book Review Editor RICHARD B. BIRRER, MD
Consulting Editor NAOMI R. BLUESTONE, MD, MPH
Consulting Editor CARL POCHEDLY, MD
Consultant in Biostatistics JOSEPH G. FELDMAN, DRPH
Managing Editor RALPH W. BATTEY
Advertising Production Coordinator KEVIN DAVEY
Copy Editor VICKI GLASER
Editorial Assistant MARYANN VIGLIOTTI
Administrative Assistant MAUREEN MAHER
Librarian ELLA ABNEY

ASSOCIATE EDITORIAL BOARD 1993

RANDALL BLOOMFIELD, MD
ROBERT D. BRANDSTETTER, MD
JOHN S. DAVIS, MD
CHARLES D. GERSON, MD
MYLES S. GOMBERT, MD
ALFRED P. INGEGNO, MD
ARTHUR H. WOLINTZ, MD
FLORENCE KAVALER, MD
JAMES M. MORRISSEY, ESQ
STEPHEN NORDLICHT, MD
JOSEPH SCHLUGER, MD
RICHARD A. STEIN, MD
RODRIGO E. URIZAR, MD

Microform copies. This publication is available on microform film. Address orders to University Microfilms, 300 North Zeeb Road, Ann Arbor, MI 48106.

Advertising representatives. *Pharmaceutical Advertising:* Cunningham Associates, PO Box 308, Park Ridge, NJ 07656. Telephone: (201) 767-4170. *Non-Pharmaceutical Advertising:* Cookson Media Services, Inc., PO Box 3669, Trenton, NJ 08629. Telephone: (609) 393-7196.

MEDICAL SOCIETY OF THE STATE OF NEW YORK

MORTON M. KURTZ, MD, President
STANLEY A. STECKLER, MD, President-Elect
CHARLES N. ASWAD, MD, Past-President
JAMES H. COSGRIFF, JR., MD, Vice-President
GEORGE LIM, MD, Secretary
JOYCE M. MCCHESENEY, MD, Assistant Secretary
ANTONIO F. LASORTE, MD, Treasurer
STANLEY L. GROSSMAN, MD, Assistant Treasurer
SEYMOUR R. STALL, MD, Speaker
JOHN H. CARTER, MD, Vice-Speaker

Councilors

Term Expires 1993

RANDALL D. BLOOMFIELD, MD, Kings
WILLIAM A. DOLAN, MD, Monroe
ROBERT M. GEORGE, MD, Oneida
STUART I. ORSHER, MD, New York

Term Expires 1994

ROBERT BRUCE BERGMANN, MD, Nassau
RICHARD A. HUGHES, MD, Warren
JEFFREY A. RIBNER, MD, Broome
ANTHONY P. SANTOMAURO, MD, Erie

Term Expires 1995

BRUCE H. BERLIN, MD, Suffolk
ALBERT M. ELLMAN, MD, Albany
FRED N. FLATAU, MD, Queens
SANFORD A. KAPLAN, MD, Westchester

Resident Councilor (representing the Resident Physician Section)

PAUL PIPIA, MD, New York

Student Councilor (representing the Medical Student Section)

LEON HENDERSON, New York

Trustees

JAMES M. FLANAGAN, MD, Wayne
(Chairman)
JOHN A. FINKBEINER, MD, New York
SAMUEL M. GELFAND, MD, Nassau
M. THEODORE TANENHAUS, MD, Kings
CHARLES D. SHERMAN, JR., MD, Monroe
DUANE M. CADY, MD, Onondaga
ROBERT A. MAYERS, MD, Westchester

Executive Vice-President	DONALD F. FOY
Deputy Executive Vice-President	WILLIAM R. EGAN
Executive Vice-President Emeritus	GEORGE J. LAWRENCE, JR., MD
Program Director, Committee for Physicians' Health	LINDA A. LAMBERT
Director, Division of Communications	THOMAS M. DONOGHUE
Director, Division of Finance and Administration	PHILIP A. SCHUH, CPA
General Counsel	DONALD R. MOY, ESQ
Director, Division of Governmental Affairs	GERARD L. CONWAY, ESQ
Director, Division of Management Information Services	GEORGE J. ADJAMI
Director, Division of Marketing and Meeting Services	GERALD SULLIVAN
Director, Division of Membership Support Services	EUNICE M. SKELLY
Director, Division of Planning, Research, and Development	MICHAEL W. DELANEY, CAE
Director, Division of Policy Coordination	IRMA A. ERICKSON
Director, Division of Public Health and Education	PETER B. FARNSWORTH, MD
Director, Division of Scientific Publications	PASCAL JAMES IMPERATO, MD
Director, Division of Socio-Medical Economics	MARIO V. MENGHINI
Consultant	EDWARD SIEGEL, MD

The New York State Journal of Medicine (ISSN 0028-7628) is published monthly by the Medical Society of the State of New York. Copyright © 1993, Medical Society of the State of New York. Material may be photocopied for noncommercial scientific or educational use only. Special arrangements and permission are required from the author(s) of the particular article and from the editor for any other purpose. The editors of the *Journal* assume no responsibility for opinions and claims expressed in the articles contributed by individual authors.

SUBSCRIPTION INFORMATION. The annual subscription for members (\$30.00) is included in the annual membership dues. The subscription rate to nonmembers in the United States and Canada is \$40.00 (\$45.00 for all other countries). The single copy rate is \$6.00 Domestic/Canada, and \$7.00 Foreign, except for special issues. This includes postage. Change of address requests should give both the old and new address and allow six weeks for changeover.

The address for EDITORIAL, CIRCULATION, and ADVERTISING OFFICES is PO Box 5404, Lake Success, New York 11042. Telephone: (516) 488-6100.

POSTAGE. Second class postage is paid at New Hyde Park, New York, and additional mailing office. POSTMASTER: Send POD Form 3579 to New York State Journal of Medicine, PO Box 5404, Lake Success, New York 11042.

New York State Journal of Medicine

MARCH 1993 / Volume 93, Number 3



Contents

COMMENTARIES

- 155 **Ischemic stroke is predictable and preventable**
RALPH L. SACCO, MD
- 156 **Soft tissue sarcomas—Is adjuvant chemotherapy indicated?**
GUNWANT GURON, MD, ALFRED I. NEUGUT, MD, PhD
- 158 **Personal and self-directed continuing medical education**
CHARLES D. SHERMAN, JR, MD

RESEARCH PAPERS

- 159 **Quality of care problems among Medicare patients in New York State**
RAPHAEL P. NENNER, MD; PASCAL JAMES IMPERATO, MD;
THEODORE O. WILL, MPA
- 162 **Perioperative stroke after general surgical procedures**
SANDIP PARIKH, MD, JON R. COHEN, MD
- 165 **Compliance with New York State's do-not-resuscitate law at Memorial Sloan-Kettering Cancer Center—A review of patient deaths**
ROBERT I. MISBIN, MD; DANIEL O'HARE, PhD; MARGUERITE S. LEDERBERG, MD;
JIMMIE C. HOLLAND, MD

REVIEW ARTICLE

- 169 **The use of α -blockers in the management of benign prostatic hyperplasia**
FRANKLIN C. LOWE, MD, EDWARD STARK, MD

COMMITTEE REPORT

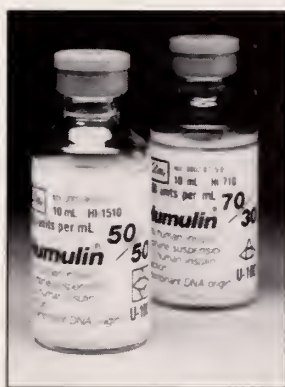
- 174 **Fetal tissue research and transplantation**
FRED ROSNER, MD; HERMAN M. RISEMBERG, MD; PIETER R. KARK, MD; PETER P. SORDILLO, MD, PhD; ALLEN J. BENNETT, MD; ANTHONY BUSCAGLIA, MD; ERIC J. CASSELL, MD; PETER B. FARNSWORTH, MD; ABRAHAM L. HALPERN, MD; JOHN B. HENRY, MD; ALLISON B. LANDOLT, MD; LAURENCE LOEB, MD; PETER ROGATZ, MD; PATRICIA J. NUMANN, MD; FERNANDO V. ONA, MD; ROBERT E. LOWENSTEIN, MD, PhD; PHILIP H. SECHZER, MD; JONATHAN R. WOLPAW, MD



Because One Size Doesn't Fit All...

New Humulin 50/50 is the tailor-made answer to individual patient needs. A unique combination of equal amounts of Regular human insulin and NPH human insulin, it will be useful in situations in which a greater initial insulin response is desirable for greater glycemic control.

Like Humulin 70/30*, new Humulin 50/50 offers the convenience and accuracy of a premix. And it can be used in conjunction with an existing 70/30 regimen.



New **Humulin** ⁵⁰/₅₀

50% human insulin
isophane suspension
50% human insulin injection
(recombinant DNA origin)

The Newest Option in Insulin Therapy

WARNING: Any change of insulin should be made cautiously and only under medical supervision.

* Humulin® 70/30 (70% human insulin isophane suspension, 30% human insulin injection [recombinant DNA origin]).



Global Excellence in Diabetes Care

Eli Lilly and Company
Indianapolis, Indiana
46285

- 200 **Remember when**
EDWIN MATLIN, MD
- 200 **Physicians in distress**
RICHARD S. GOODMAN, MD, S. KEITH LONDON, BS
- 201 **The immunization crisis in New York**
PETER B. FARNSWORTH, MD, GUTHRIE S. BIRKHEAD, MD
- 202 **Lead screening**
LUCILLE ROSENBLUTH, MPA, MILDRED A. MOREHEAD, MD
- 202 **Münchausen syndrome**
STEPHEN P. LICATA, PhD; LESLIE A. MCCLOSKEY; CAROL L. KARMEN, MD; BRUCE D. LOGAN, MD; JOHN T. FLYNN, MD

ESSAY REVIEWS

- 204 **When others must choose: Deciding for patients without capacity**
JOSEPH J. FINS, MD
- 206 **A long lost manuscript on the Peruvian bark**
PASCAL JAMES IMPERATO, MD

207 BOOK REVIEWS

- 211 OBITUARY LISTINGS
- 214 REFEREES
- 13A MEDICAL MEETINGS AND LECTURES



COMMENTARIES

Ischemic stroke is predictable and preventable

Stroke continues to be a major public health problem ranking in the top four causes of death in the United States. Stroke is more often disabling than fatal, and results in enormous costs measured in both health-care dollars and lost productivity. Surveys have documented that it is one of the most-feared complications of aging. A major aim set by the Public Health Service among the National Health Promotion and Disease Prevention Objectives for the year 2000 is "to reduce stroke deaths to no more than 20 per 100,000."¹ The most likely means of achieving these reductions in stroke morbidity and mortality are from the identification and control of environmental factors in the stroke-prone individual.

Over the past few decades, numerous conditions which elevate the risk of stroke known as "risk factors" have been identified. Some are clearly not alterable, such as age, gender, heredity and race-ethnicity. Unanswered questions regarding the importance of these demographic factors remain the subject of ongoing studies, in particular the explanation for the increased stroke mortality among African-Americans and the largely unknown stroke epidemiology among our rapidly growing Latino populations.² Population-based epidemiological investigations in ethnically mixed regions have been initiated to characterize the incidence of stroke and the relative frequency of different stroke subtypes, as well as determine the importance of stroke risk factors and evaluate prognosis after stroke in the different race/ethnic groups. Elucidating differences in these subgroups in stroke incidence and risk factors is the first step in planning effective multi-ethnic prevention programs aimed at concentrated risk factor modification.

Other stroke risk factors are quite modifiable and are the cornerstones of current strategies to prevent stroke. On the basis of the results of case-control and prospective cohort studies, definite stroke risk factors have been identified: hypertension, cardiac disease (particularly atrial fibrillation), diabetes, hypercholesterolemia, cigarette use, alcohol abuse, transient ischemic attacks and prior stroke. More recently, improved cardiac imaging has led to the increased detection of potential stroke risk factors such as mitral valve prolapse, patent foramen

ovale,³ aortic arch disease, atrial septal aneurysms, and spontaneous echo contrast. Various laboratory abnormalities, often reflecting an underlying metabolic or hematological disturbance, have been associated with stroke and identified as possible stroke precursors. These include hematocrit, polycythemia, sickle cell anemia, white blood count, fibrinogen, hyperuricemia, hyperhomocysteinemia, protein C and free protein S deficiencies, Lupus anticoagulant, and anticardiolipin antibodies. Some are clear stroke risk factors, whereas others require confirmation and clarification.

Stroke risk factors are multiple and additive. Stroke-prone profiles have been developed from the Framingham Study which can be used to estimate the risk of stroke for a person given a combination of factors.⁴ For example, a 70-year-old woman with a systolic blood pressure of 180 mm Hg despite being on antihypertensive medications who is diabetic and smokes cigarettes has an estimated ten-year probability of stroke of 37%, over 3× greater than the average risk for a woman at age 70. Identifying the independence of certain risk factors and the co-dependence of others are important in estimating the probability of stroke. The risk of stroke can be estimated in a variety of circumstances and help with decisions regarding risk factor modification or weighing the risks and benefits when planning a surgical procedure.

In this issue of the *Journal*, Parikh and Cohen⁵ report a case-control study to identify the preoperative, intraoperative and postoperative factors associated with perioperative stroke following general and vascular surgical procedures. The significant contributors were hypertension, smoking, prior neurological symptoms and an abnormal rhythm on electrocardiogram (atrial fibrillation). Carotid bruit was not a significant predictor, but statistical power was limited. On the basis of the results of their study, perioperative stroke is potentially predictable. The method to modify the risk of stroke and prevent perioperative stroke remains a challenge.

The results from five recent randomized trials have helped guide the management of persons with non-valvular atrial fibrillation.⁷ For this high-risk group

warfarin has proved superior to placebo or aspirin for prevention of stroke. Reductions in the risk of thromboembolic events have been great and the relative cost in terms of hemorrhagic side-effects have been smaller than previously feared. For now, as suggested by Parikh and Cohen, perioperative anticoagulation is probably warranted among those with atrial fibrillation who are in need of surgery.⁵ The Stroke Prevention in Atrial Fibrillation study is continuing to compare warfarin to aspirin in persons under age 75. Moreover, a clinical trial comparing warfarin to aspirin is also underway regarding the prevention of recurrent stroke among patients with non-cardioembolic stroke (Warfarin Aspirin Recurrent Stroke Study).

Surgical clinical trials have documented that carotid endarterectomy is of proven efficacy among persons with transient ischemic attack (TIA) or minor stroke and an ipsilateral carotid stenosis of 70% or more. One must agree with the suggestions of Parikh and Cohen that part of the preoperative assessment in persons with prior neurological symptoms should include a carotid duplex Doppler and consideration of endarterectomy among those who have symptomatic carotid stenosis greater than 70%.⁵ The benefits of endarterectomy are unproven, however, in those with symptoms and 40%–69% stenosis or among those with asymptomatic carotid stenosis. The answers to the latter questions should be known within the next few years with the completion of ongoing studies. Until such time, continued randomization in the North American Symptomatic Carotid Endarterectomy Trial (NASCET) or Asymptomatic Carotid Artery Surgery Study (ACASS) seems prudent.

Antiplatelet agents have been found to be effective in reducing the stroke risk in persons with transient ischemic attack or stroke. Aspirin is well-known and accepted because of the proven efficacy compared with placebo, safety and low cost, but the risk reductions in randomized trials are marginal. Controversies continue regarding the most effective dose; the reduction of gastrointestinal bleeding and side effects with lower doses is documented. The efficacy of aspirin and/or subcutaneous heparin in acute ischemic stroke is being studied in a worldwide collaborative effort as part of the International Stroke Trial. The latest Food and Drug Administration (FDA) approved antiplatelet agent, Ticlopidine, is more effective than placebo and aspirin in

reducing cerebrovascular risks, but the small risk of neutropenia require adherence to a monitoring program. Other agents are being developed and tested in phase II and III trials for acute ischemic stroke, as well as long-term stroke prophylaxis.

In spite of the multitude of identified stroke risk factors, there are still a large proportion of strokes that defy adequate explanations and are classified as cryptogenic stroke.⁸ To decrease the number labeled as cryptogenic, further epidemiological studies are needed to identify and characterize new determinants of stroke. Strategies to modify and treat these factors can then be developed and subjected to the rigor of the randomized clinical trial. The future will call for selective stroke therapies based on the risk factor subgroup and preoperative treatment with neuroprotective agents in identified high stroke-risk individuals. Even the smallest reduction in stroke incidence could translate into a savings of thousands of lives and minimize the threat of early disability among our aging population. In the years ahead there is much more work to be done if we are to meet the goals of Healthy People 2000.

RALPH L. SACCO, MD,
Assistant Professor of Neurology
and Public Health (Epidemiology)
in the Gertrude H. Sergievsky Center
Columbia University College of Physicians and Surgeons
Director
Northern Manhattan Stroke Study
Neurological Institute
Columbia University College of Physicians and Surgeons
710 W 168 St
New York, NY 10032

1. Healthy People 2000, 1990, DHHS Publication No (PHS) 91-50213.
2. Sacco RL, Hauser WA, Mohr JP: Hospitalized stroke in blacks and Hispanics in northern Manhattan. *Stroke* 1991; 22:1491–1496.
3. DiTullio MR, Sacco RL, Gopal AS, et al: Patent foramen ovale as a risk factor for cryptogenic stroke. *Ann Intern Med* 1992; 117:461–465.
4. Wolf PA, D'Agostino RB, Belanger AJ, et al: Probability of stroke: a risk profile from the Framingham Study. *Stroke* 1991; 22:312–318.
5. Parikh S, Cohen JR: Perioperative stroke following general surgical procedures. *NY State J Med* 1993; 93:162–165.
6. SHEP Cooperative Research Group: Prevention of stroke by antihypertensive drug treatment in older persons with isolated systolic hypertension: final results of the Systolic Hypertension in the Elderly Program (SHEP). *JAMA* 1991; 265:3255–3264.
7. Laupacis A, Albers G, Dunn M, et al: Antithrombotic therapy in atrial fibrillation. *Chest* 1992; 102:426S–433S.
8. Sacco RL, Ellenberg JA, Mohr JP, et al: Infarction of undetermined cause: the NINCDS stroke data bank. *Ann Neuro* 1989; 25:382–390.

Soft tissue sarcomas

Is adjuvant chemotherapy indicated?

Soft tissue sarcomas (STS) are uncommon malignancies of mesodermal embryologic origin with a variety of histologic types including leiomyosarcomas, liposarcomas, malignant fibrous histiocytomas and rhabdomyosarcomas. As a group, they constitute 1% of adult malignancies and 15% of pediatric malignancies.¹

Leiomyosarcomas (LMS) are basically tumors of smooth muscles and constitute 5%–9% of adult soft

tissue sarcomas. The most common sites of occurrence are the extremities, but they also arise from smooth muscle in the viscera, especially the gastrointestinal tract, uterus, retroperitoneum, or smooth muscles in the vascular tissue. They usually present as a mass at the primary site but other presentations, such as multiple cranial nerve palsies or para-neoplastic syndromes, can be seen with this type of STS.²

In this issue of the *Journal*, an unusual case of bilateral high-grade LMS of the lower extremities is reported by Berinstein et al.³ It developed six months following diagnosis of a rectal cancer, treated with abdominoperineal resection and radiation therapy. Most probably this represents a chance occurrence of two malignancies. While there are some reported associations of STS with second malignancies, only one study has shown an association with colon cancer in the same individual.⁴ This same study found no association between rectal cancer and STS. On the other hand, it is well known that in families with Li-Fraumeni syndrome there is an increased number of individuals with sarcomas, breast carcinomas and other tumors.¹ It would of interest to know the patient's family history especially with regard to p53 germline mutations.

The LMS in this patient was treated with excisional biopsy followed by wide local excision and adjuvant radiation therapy (RT). In spite of aggressive local treatment of primary lesions, there is a significant rate of both local recurrence and distant metastasis in high-grade tumors. Although there have been improvements in outcome over the last two decades, currently most patients with high-grade lesions die of recurrent metastatic disease within five years. Hence, adjuvant chemotherapy has been offered to these patients to sterilize occult micro-metastases.

Tumor grade is the single most important prognostic factor in STS, but there is some difficulty with the reproducibility of grade among different pathologists. Assessment of grade is a complex task, incorporating the number of typical and atypical mitoses per high-power field, and the degree of spontaneous necrosis and pleomorphism. Other prognostic factors include tumor size (greater or lesser than 5 cm), the extent of the surgical margins and the presence or absence of vascular invasion.⁵

Is LMS distinct from other soft tissue sarcomas? It has been shown that, grade for grade, there is no difference in outcome in different pathologic subtypes.⁶ Tumor grade has proven to be more important than histopathology in predicting biologic behavior.

In low-grade sarcomas, adjuvant chemotherapy is not indicated because of the low probability of metastatic disease and the significant toxicity related to treatment. Doxorubicin and ifosfamide are the most active single agents in STS.⁷ Doxorubicin has been used alone or in combination with cyclophosphamide, vincristine, dactinomycin, and DTIC. Responses are seen in 35% of cases. At the Dana-Farber Cancer Institute the combination of doxorubicin, ifosfamide, and DTIC has shown an overall response rate (RR) of 50%.⁷

Twelve randomized trials of adjuvant chemotherapy in STS have been reported. The largest trial is from the EORTC in which 468 patients with complete resection of primary tumor were randomized to CYVADIC (cyclophosphamide, vincristine, doxorubicin, and dacarbazine) given every four weeks versus observation.⁸ After a follow-up of 44 months there was no difference in either disease-free or overall survival. A smaller study from Bordeaux,⁹ using identical doses of CYVADIC, showed a significant advantage for chemotherapy in preventing local recurrence and in disease-free and

overall survival. However, this study had just 59 patients and there was a significant imbalance of patients, with more extremity sarcomas in the chemotherapy arm. An Italian study in which 77 patients with high-grade extremity lesions were randomized to doxorubicin versus observation showed a statistically significant difference in survival for the chemotherapy arm as well.¹⁰

Results from other randomized studies conducted by the Scandinavian Sarcoma Group, the Intergroup Sarcoma Study (Dana-Farber Cancer Institute, Massachusetts General Hospital, Eastern Cooperative Oncology Group), and the Gynecologic Oncology Group have not shown any statistically significant differences in the control arm versus chemotherapy arm in either disease-free or overall survival.⁷ These studies used doxorubicin at doses of 60–70 mg/m² versus no chemotherapy.

At the National Cancer Institute (NCI), patients with STS (both extremity and non-extremity) were randomized to observation versus doxorubicin and cyclophosphamide followed by six monthly cycles of high-dose methotrexate with leucovorin rescue.¹ Subset analysis for extremity patients revealed a significant improvement in disease-free and overall survival for the chemotherapy arm at a median follow-up time of five years, although at seven years there was no difference in overall survival for the two arms. Similarly, studies from the Mayo Clinic and MD Anderson Cancer Center have not shown a significant difference in overall survival in the chemotherapy versus control arms.^{12,13}

Of the 12 published randomized studies, only two showed a significant overall survival advantage for the chemotherapy arm.^{9,10} Doxorubicin, which is the most commonly used chemotherapeutic agent, has significant cardiotoxicity (seen in 10% of treated patients) and can occasionally result in treatment related death. Low-grade sarcomas are cured by surgical resection in 80% of cases and should not be included in adjuvant trials.

Adjuvant chemotherapy has proven to be useful for rhabdomyosarcomas.⁷ However, for other histologic categories of STS, randomized trials are indicated for patients with large, high-grade tumors. Thus, the patient described by Berinstein et al in this issue of the *Journal* might have benefitted from an investigational study, were one available.⁴

GUNWANT GURON, MD
Post Doctoral Clinical Fellow

ALFRED I. NEUGUT, MD, PhD
Associate Professor of Clinical Medicine
and Public Health
Department of Medicine
Columbia University
College of Physicians and Surgeons
630 West 168th Street
New York, NY 10032

1. Mazanet R, Antman KH: Sarcomas of soft tissue and bone. *Cancer* 1991; 68:463–473.

2. Kiu MC, Liaw CC, Ng KT: Leiomyosarcoma associated hypoglycemia. *Chang-Keng-I-Hsueh* 1990; 13:237–241.

3. Berinstein D, Godizez J, Kimmel R, et al: Bilateral, symmetrical leiomyosarcoma of the lower extremities: case report and review. *NY State J Med* 1993; 93:194–195.

4. Schoenberg BS: Multiple primary malignant neoplasms: the Connecticut experience, 1935–1964. Berlin, New York, Springer-Verlag, 1977, pp 123–146.

5. Antman KH, Eilber FR, Shiu MH: Soft tissue sarcomas: current trends in diagnosis and management. *Curr Probl Cancer* 1989; 6:340–367.

6. Suit HD, Russell WO, Martin RG: Sarcoma of soft tissue: clinical and histopathologic parameters and response to treatment. *Cancer* 1975; 35:1478-1483.
7. Mazanet R, Antman KH: Adjuvant therapy for sarcomas. *Sem Oncol* 1991; 18:603-612.
8. Bramwell V, Rouesse J, Steward W, et al: European experience of adjuvant chemotherapy for soft tissue sarcoma: interim report of a randomized trial of CYVADIC versus control. In: *Recent Concepts in Sarcoma Treatment*. Dordrecht, Netherlands, Kluwer Academic 1988, pp157-164.
9. Ravaud A, Nguyen BB, Coundre JM, et al: Adjuvant chemotherapy with CYVADIC in high risk soft tissue sarcoma. In: *Adjuvant Therapy of Cancer*, V1. Philadelphia, P.A. Saunders, 1990, pp556-566.
10. Picci P, Bacci G, Gherlinzoni F, et al: Results of a randomized trial for the treatment of localized soft tissue tumors of the extremities in adult patients. In: *Recent Concepts in Sarcoma Treatment*. Dordrecht, Netherlands, Kluwer Academic, 1988, pp144-148.
11. Chang A, Kinsella T, Glatstein E, et al: Adjuvant chemotherapy for patients with high-grade soft tissue sarcomas of the extremities. *J Clin Oncol* 1988; 6:1491-1500.
12. Edmondson JH, Flemming TR, Ivins JC, et al: Randomized study of systemic chemotherapy following complete excision of non-osseous sarcomas. *J Clin Oncol* 1984; 2:1390-1396.
13. Benjamin RS, Terjanian TO, Fenoglio CJ, et al: The importance of combination chemotherapy for adjuvant treatment of high-risk patients with soft-tissue sarcomas of the extremities. In Salmon SE (ed): *Adjuvant Therapy of Cancer*, V. Orlando FL, Grune and Stratton, 1987, pp735-744.

Personal and self-directed continuing medical education

The best education, including continuing medical education (CME), is personal and self-directed. The role of the educator should be as a "facilitator" for this personal and self-directed process, and "accredited providers" of education, should build upon this concept as much as possible. Unfortunately, the vast bulk of CME still consists of lectures or courses of lectures designed by the accrediting organizations with little or no input from the individual participants or consumers of CME. Furthermore, the lecture has been heavily down-graded by most educators as being relatively ineffective, and indeed, many medical schools have significantly cut their lectures by 50% or more, building on the concept that interactive learning where the student is actively involved in his own education should be substituted as much as possible for the passive lecture system. Even when one tries to make a lecture interactive by allowing half of the time for discussion, the interaction never involves more than a small percentage of the learners and the discussion is rarely organized for maximal effectiveness.

While a few CME providers are using these concepts for a small proportion of their CME activities, all of us in the CME enterprise must work strenuously to make this proportion 85%-90% rather than 5%. We need many more pilot projects in which CME providers work with individual learners to determine educational needs germane to their individual practice. The provider then serves as a facilitator for the indicated learning activities.

Such pilot projects may initially require more resources, but in the long run should become extremely "cost effective," simply because it is truly personal and self-directed. The change from being providers of CME courses to being "facilitators" of individualized learning would be a giant step for all of us.

Unfortunately, the bureaucracy of CME is increasing rather than decreasing, using up more and more of the available resources. The mammoth job of acquiring and keeping track of CME credits from numerous courses of lectures provided by many different organizations is, in my opinion, counterproductive and largely a public relations effort to show the public that the profession is committed to keeping up-to-date. The increased monitoring activities of all CME programs to guarantee to the FDA and others that CME meets the essentials and is not commercial promotion of the pharmaceutical industry's offering will use up still more of our resources, increase the bureaucracy, and draw attention further away from the more important kinds of CME noted above.

To summarize, the key elements in our CME enterprise in the 90s should be the following: personal, self-directed, interactive, individualized learning with the providers becoming facilitators of the process. The bureaucracy of CME must be minimized!

CHARLES D. SHERMAN, JR, MD
Highland Hospital
1000 South Avenue
Rochester, NY 14620

Quality of care problems among Medicare patients in New York State

RAPHAEL P. NENNER, MD; PASCAL JAMES IMPERATO, MD; THEODORE O. WILL, MPA

ABSTRACT. The Island Peer Review Organization is the peer review organization in New York State and is under contract with the Health Care Financing Administration to monitor the quality of care rendered to Medicare patients. A severity level III is assigned when a confirmed quality problem with significant adverse effects for the patient is confirmed. A severity level II is assigned when a confirmed quality problem with the potential for significant adverse effects on the patient is found.

The purpose of this study was to retrospectively analyze all 85 severity level III citations and a 12% (223) random sample of the 1,880 severity level II citations for 1991. Another objective was to characterize the providers involved in each of these two levels of quality of care problems.

Among the 85 severity level III citations, 34 (40.0%) involved premature death and 33 (38.8%) readmission. Treatment (45.0%), diagnostic (16.9%), and monitoring (16.4%) problems accounted for 78.3% of the 189 problems identified in severity level III citations. The leading problem areas were the treatment of infections and the use of antibiotics (21.2%), fluid and electrolyte management (21.2%), drug use (9.4%), the use of endotracheal tubes (5.9%), the management of diabetes mellitus (5.9%), and the management of hematologic disorders (5.9%). Attending physicians (65.9%), nursing departments (16.5%), and resident physicians (7.1%) were involved in the vast majority (89.5%) of severity level III citations.

Treatment problems comprised 60.5% of the 243 problems found in severity level II citations, followed by inadequate work-up (20.2%), and incomplete documentation (12.3%). The major problem areas identified among severity level II citations included the treatment of infections and antibiotic use (22.4%), poor discharge planning and premature discharge (13.9%), drug use (11.2%), fluid and electrolyte management (9.4%), the management of diabetes mellitus (4.5%), and the management of hematologic disorders (3.6%). Attending physicians (74.4%) and nursing departments (18.4%) were responsible for the vast majority (92.8%) of severity level II citations.

The results of this study indicate that a significant proportion of severity level III and severity level II citations are due to diagnostic, treatment, and monitoring problems regarding several discrete medical care areas. These include the treatment of infections and antibiotic use, fluid and electrolyte management, drug use, the management of diabetes mellitus, and the management of hematologic disorders.

Educational interventions should be extended to physicians, nurses, and other providers and focused on identified major areas of quality of care problems, such as those identified in this study. This should lead to a significant reduction in the frequency of quality problems with either significant adverse effects (level III) or the potential for significant adverse effects (level II) on patients.

(NY State J Med 1993; 93:159-162)

The Island Peer Review Organization (IPRO) is a New York State peer review organization which since 1989 has been under contract to the Health Care Financing Administration (HCFA) and the New York State Department of Health, respectively performing Medicare and Medicaid reviews. In recent years, IPRO has conducted an annual average of 150,000 retrospective Medicare medical chart reviews, and over 100,000 acute Medicaid and alternate level of care reviews.

IPRO randomly examines approximately 19 percent of all annual Medicare hospitalizations in New York State to determine the appropriateness of the medical care rendered and the resources utilized. Selected criteria are employed as requested by HCFA, such as re-admission, ambulatory care, exempt unit admissions, and so forth. The first step in this process consists of review by trained nurse reviewers who use the generic quality screens provided by HCFA in order to evaluate the quality of care given. When it is found that the medical care in a particular case fails to meet the criteria of the generic quality screens, a physician consultant conducts a thorough review of the chart. The review process is ended if the physician reviewer finds no quality issues. However, if a determination is made that a quality of care problem exists, an inquiry is sent to the attending physician and/or hospital, requesting additional information from them. Once the providers furnish the additional information, a second physician consultant (specialist) determines whether or not quality problems exist and those responsible for them. At this time, the severity levels of the quality problems are determined according to HCFA definitions (Table I) (in all level III citations, the IPRO medical director reviews the chart prior to sending the inquiry to the provider). These severity levels, assigned by IPRO, are uniform and nationwide in character as they have been established by HCFA.

A significant adverse effect is defined as unnecessarily and significantly prolonged treatment, serious medical complication(s), avoidable readmission, serious physiological or anatomical impairment, significant disability, and/or avoidable death. Acute hospital readmissions due to premature discharges are considered significant adverse effects

From the Island Peer Review Organization (IPRO), Lake Success, NY. Raphael P. Nenner, MD and Theodore O. Will, MPA (IPRO); Pascal James Imperato, MD (IPRO and Department of Preventive Medicine and Community Health, State University of New York Health Science Center at Brooklyn, NY).

Address correspondence to Dr Nenner, Vice President for Medical Affairs, Island Peer Review Organization, 1979 Marcus Ave, Lake Success, NY 11042.

TABLE I. Severity Level of Quality Problems

Severity Level	Definition*
Level I	A confirmed quality problem without the potential for significant adverse effects on the patient.
Level II	A confirmed quality problem with the potential for significant adverse effects on the patient.
Level III	A confirmed quality problem with significant adverse effects on the patient.

*Significant adverse effect is defined as unnecessarily and significantly prolonged treatment, complications, or hospital readmissions, or as patient mismanagement which results in anatomical or physiological impairment, disability or death.

(severity level III) because a patient who exhibits signs and/or symptoms severe enough to require treatment as an inpatient in an acute hospital certainly requires "significant-prolonged treatment."

In determining the appropriate severity level assignment, there are certain facts which are considered:

- the existence of a deficiency does not necessarily result in an "adverse effect."
- To be considered a quality problem, an "adverse effect" must be a direct result of an identified deficiency.

IPRO has on its roster physician consultants of whom more than 300 conducted Medicare reviews in 1991. As a prerequisite to becoming a physician consultant, many of them attend two training seminars annually. Ninety-one percent of IPRO's consultants are board-certified physicians. The majority have academic appointments, and all of the physician consultants were recommended by the respective chairman of their division review committee (geographical area where the physician practices). Many physician consultants were monitored in 1991, with a goal that eventually all physician consultants be monitored by either their peers and/or a senior physician consultant/medical director.

These formal monitorings are also reviewed by IPRO's Vice President for Medical Affairs and are computerized. In cases where there is a disagreement or partial agreement, there is an exchange and/or discussion between the physician consultant and the medical director. Because of the nature of reviews, specific processes must be adhered to as dictated by HCFA. Some physician consultants are counselled, given personal attention, and training. If there is a disagreement between an attending physician and a physician consultant, a senior physician consultant (who is always board certified in the specialty of the attending physician) will render a final decision. In cases where a disagreement still exists, the case is referred to the Quality Assurance Committee (upstate or downstate) for final determination. The members of the Quality Assurance Committee (one upstate; two downstate) are staffed by specialists in different subspecialties.

The purpose of this study was to analyze the level II and level III quality problems observed among hospitalized Medicare patients in New York State in 1991. Another objective was to characterize the provider types involved in each of these two levels of quality of care problems.

METHODS

In 1991, IPRO processed 1,081,153 Medicare claims of which 203,046 (18.8%) were evaluated for quality of care through the use of generic quality screens. Of these, 1,804 were determined to be severity level I, 1,880 severity level II, and 85 severity level III. The review documents and correspondence

for all of the level IIIs and for a 12% (223) random sample of the level IIs were carefully analyzed. Information from the original data base and the review documents was incorporated for each citation on to a quality study data instrument that included essential identifying information and categories of quality problems. The latter were grouped under six broad areas including incomplete documentation, inadequate work-up, diagnosis, treatment, monitoring failure and outcome. The information on the data instruments was then computer coded and analyzed.

RESULTS

Level III Problems. There were a total of 189 problems found among the 85 level III citations, making for an average of 2.2 per citation. As shown in Figure 1, treatment problems comprised 45.0% of the total, it being inadequate in 27.0% and inappropriate in 11.1%. Treatment problems were followed in frequency by those involving diagnosis (16.9%) and monitoring failures (16.4%). Incomplete diagnoses (13.8%) were more than four-fold more frequent than inadequate ones (3.1%). Monitoring failures primarily involved laboratory results (9.0%). An inadequate work-up was present in 13.2% of citations and incomplete documentation in 8.5%. With regard to outcome, premature death occurred in 34 (40.0%) of citations and readmissions in 33 (38.8%).

Diagnostic, treatment, work-up, and monitoring problems in each of the 85 citations were closely studied to determine the most important ones which resulted in a severity level III citation. The five leading problem areas were found to be treating infections and the use of antibiotics (21.2%), fluid and electrolyte management (21.2%), inappropriate drug use (9.4%), the use of endotracheal tubes (5.9%), and the management of diabetes mellitus (5.9%) (Table II).

The distribution of provider type involved in severity level III citations is shown in Figure 2. Attending physicians were involved in the vast majority (65.9%), followed by nursing departments (16.5%), and resident physicians (7.1%).

Level II Problems. There were a total of 243 problems found among the 223 severity level II citations, making for an average of 1.1 per citation. Treatment problems comprised 60.5% of the total and were three times as frequent as the next most common problem, inadequate work-up, which was found in 20.2%. Incomplete documentation (12.3%), monitoring failures (3.7%), and diagnostic problems (3.3%) followed in frequency (Figure 3).

Diagnostic, treatment, work-up, and monitoring problems in each of the 223 citations were further analyzed to elucidate the nature of these problems. As with the severity level III citations, treating infections and the use of antibiotics, inappro-

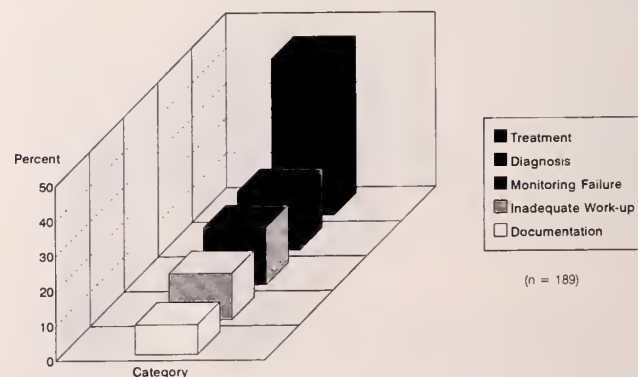


FIGURE 1. Distribution of Medicare severity level III quality problem categories, 1991.

TABLE II. Distribution of Common Medicare Severity Level III Quality Problems, 1991 (n = 85)

Problem	Number	Percentage
Treating infections and the use of antibiotics	18	21.2
Fluid and electrolyte management	18	21.2
Inappropriate drug use	8	9.4
Use of endotracheal tubes	5	5.9
Management of diabetes mellitus	5	5.9
Management of hematologic disorders	5	5.9
Placement and use of nasogastric tubes	4	4.7
Falls and injuries due to inadequate patient supervision	3	3.5
Management of cardiac problems	3	3.5
Management of gastro-intestinal bleeding	3	3.5
Failure to recognize pacemaker problems	2	2.4
Unnecessary surgery	2	2.4
Inadequate surgery	1	1.2
Other	8	9.4
TOTAL	85	100.00

appropriate drug use, and fluid and electrolyte management problems were among the leading areas of deficiency (Table III).

Poor discharge planning and premature discharge were third in frequency and the management of diabetes mellitus sixth (4.5%). As shown in Table III, six (2.7%) patients had inadequate work-ups prior to cataract surgery. In five (2.2%) patients the history and physical examination were either non-existent or inadequate. In another five (2.2%), there were problems with the use of digitalis preparations and with the monitoring of digitalis levels and in 4 (1.8%) problems with the use of dilantin and in monitoring dilantin levels.

The distribution of provider type involved in severity level II citations is shown in Figure 4. As with severity level III citations, attending physicians (74.4%) and nursing departments (18.4%) were involved in the vast majority of citations. Problems involving the hospital occurred in 4.5% and resident physicians were only involved in 1 (0.4%) citation.

DISCUSSION

The results of this retrospective epidemiologic study show that treatment problems are the most frequent reasons for both severity level III and severity level II citations. They comprise 45.0% of level IIIs and 60.5% of level IIs. In both categories of citations, problems with treating infections and antibiotic use, fluid and electrolyte management, drug use, and the management of diabetes mellitus are among the most frequently observed. The similar distribution of these most frequent problems for both severity levels reflects in part a consistency in the

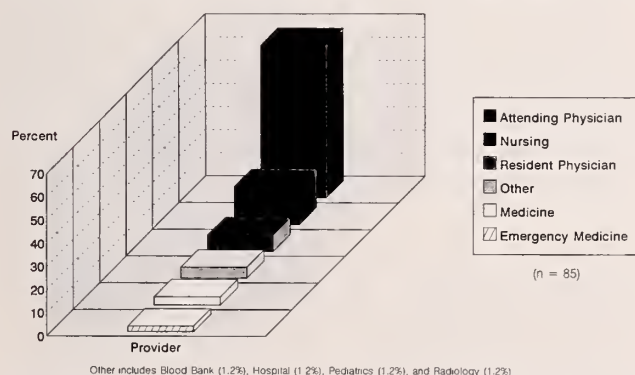


FIGURE 2. Distribution of provider type among Medicare severity level III quality problems.

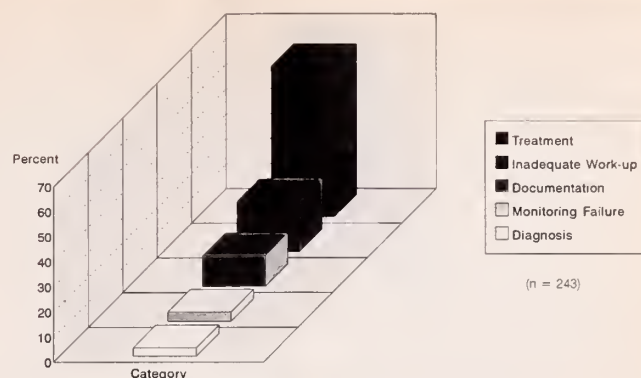


FIGURE 3. Distribution of Medicare severity level II quality problem categories, 1991.

application of HCFA standards during the review process. This process, summarily reviewed earlier in this communication is also detailed elsewhere.¹

Attending physicians were found to be the providers most frequently responsible for citations, accounting for 65.9% of severity level IIIs and 74.4% of severity level IIs. They are followed by the nursing department which accounted for 16.5% and 18.4% respectively. It is important to note that resident physicians accounted for 7.1% of severity level III citations.

A recent study by California Medical Review, Inc, which is the peer review organization for that state's 3.36 million Medicare patients, showed a similar proportional distribution of severity level III and severity level II citations.² Leape et al have shown that among nonoperative adverse events involving negligence among hospitalized patients in New York State, drug related, diagnostic, and therapeutic mishaps occur with significant frequency.³

Brennan et al conclude from their study of hospitalized patients in New York State that there is a substantial amount of injury to patients from medical management and

TABLE III. Distribution of Common Medicare Severity Level II Quality Problems, 1991 (n = 223)

Problem	Number	Percentage
Treating infections and the use of antibiotics	50	22.4
Other	37	16.6
Poor discharge planning and premature discharge	31	13.9
Inappropriate drug use	25	11.2
Fluid and electrolyte management	21	9.4
Management of diabetes mellitus	10	4.5
Management of hematologic disorders	8	3.6
Falls and injuries due to inadequate patient supervision	8	3.6
Failure to perform adequate pre-operative work-up on patients undergoing cataract surgery	6	2.7
Problems with the use of digitalis and in monitoring digitalis levels	5	2.2
Management of cardiac problems	5	2.2
Inadequate or no history or physical examination in chart	5	2.2
Problems with the use of dilantin and in monitoring dilantin levels	4	1.8
Failure to document blood pressure on chart	4	1.8
Placement and use of nasogastric tubes	4	1.8
TOTAL	223	100.00

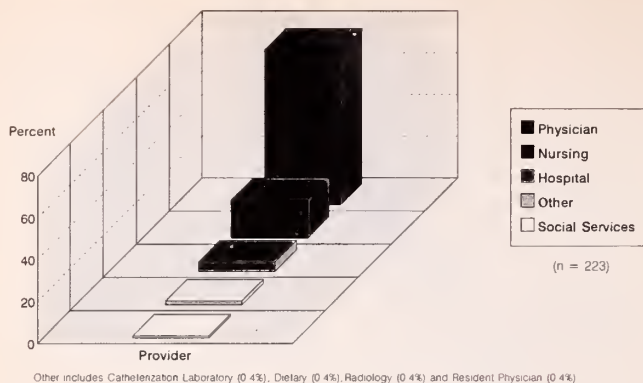


FIGURE 4. Distribution of provider type among Medicare severity level II quality problems.

that many injuries are the result of substandard care. They also found that the rate of adverse events due to negligence rose with age and that it was markedly higher among the elderly.⁴ The population reviewed in this current study is largely an elderly one in whom adverse events are more likely to occur because of numerous co-morbidities. However, adverse events alone are not a measure of poor quality care, nor is their absence indicative of good quality care. Levels II and III are assigned not only because there is an adverse effect, but also, and most importantly, because the adverse effect is due to a confirmed quality of care problem.

It is of great concern that death directly resulted from confirmed cited problems in 34 (40.0%) of the 85 level III citations. These deaths were avoidable and were directly due to departures from accepted standards of medical care.

Also of concern is the fact that in 33 (38.8%) level III citations, readmission resulted from confirmed quality problems in the previous admission.

If educational interventions are to be used to improve the quality of care problems documented in the present study, they must be directed to several types of providers, but especially to physicians and nurses. Focused educational interventions in the subject areas of treating infections and antibiotic use, fluid and electrolyte management, drug use, the management of diabetes mellitus and the management of hematologic disorders would most likely yield significant improvements in the quality of care problems since problems in these areas accounted for 63.6% of level III and 51.1% of level II citations.

Acknowledgments. We wish to acknowledge the assistance and suggestions of Charles M. Alcorn, ScD; Harriet Starr, MA, Vice President, Management Information Systems, the Island Peer Review Organization (IPRO), Gary B. Beringer, DRPH, Director, Department of Data Analysis, IPRO, John Zetzsche, MA, Research Analyst and H. Peter Lee, SB, Research Analyst, IPRO. We wish to thank Michael S. Muller, MA, Senior Research Analyst, IPRO, for designing and producing the figures.

REFERENCES

1. Nenner RR: A physician's guide to quality review. *NY State J Med* 1991; 91:157-159.
2. California Medical Review, Inc.: A Summary of Operations: *Third Scope of Work*, April 1, 1989-March 31, 1992, San Francisco, CMRI, 1992.
3. Leape LL, Brennan TA, Laird N, et al: The nature of adverse events in hospitalized patients. Results of the Harvard Medical Practice Study II. *N Engl J Med* 1991; 324:377-384.
4. Brennan TA, Leape LL, Laird NM et al: Incidence of adverse events and negligence in hospitalized patients: results of the Harvard Medical Practice Study I. *N Engl J Med* 1991; 324:370-376.

Perioperative stroke after general surgical procedures

SANDIP PARIKH, MD, JON R. COHEN, MD

ABSTRACT. Perioperative cerebrovascular accidents after general surgical procedures are rare, but devastating and often fatal. The purpose of this study was to identify the perioperative, intraoperative, and postoperative factors associated with perioperative strokes after general surgical procedures. Over a five-year period, 19 patients of 24,641 general and vascular surgical procedures (0.08%) suffered a perioperative stroke. Patients undergoing carotid endarterectomies were excluded. These 19 patients were compared with a group of 19 patients matched for age and procedure. The strokes occurred in relation to the surgery as follows: 53% within 24 hours, 31% within one to seven days, and 16% within seven to thirty-six days. The overall perioperative mortality was 26%. In long-term follow-up, four patients died, two had complete recovery (11%), two had 90% recovery (11%), one had partial recovery (5%), and one remained completely disabled (5%). In comparing the groups, the

significant factors contributing to perioperative stroke included hypertension, smoking, earlier neurological symptoms, and an abnormal rhythm on electrocardiogram. The most common factor for stroke was atrial fibrillation. Only one patient had an intracerebral hemorrhage.

Although the exact mechanism of perioperative stroke remains uncertain, its association with abnormal cardiograms, lack of association with carotid bruits, and lack of intracerebral hemorrhage all suggest that emboli from the heart is the major cause in most patients. These data indicate that a perioperative stroke is associated with a very high mortality rate (26%) and is a potentially predictable complication in the majority of patients.

(*NY State J Med* 1993; 93:162-165)

Perioperative cerebrovascular accidents (CVA) after general surgical procedures are rare, but devastating and often fatal. Postoperative stroke more commonly occurs after cardiac and carotid artery surgery with an incidence of approximately 2%-5%.¹ Stroke after general surgical procedures is reported to be less than 1%^{2,6} and in elderly

From the Department of Surgery Long Island Jewish Medical Center, New Hyde Park, NY.

Address correspondence to Dr Cohen, Department of Surgery, Long Island Jewish Medical Center, New Hyde Park, NY 11042.

patients to be approximately 1%.³ Patients undergoing aorta-iliac surgery are thought to be at a special risk for perioperative stroke because of the high prevalence of coexistent carotid disease; however, the perioperative stroke rate is reported to be only 1%.^{4,5}

Little is known about the mechanism of perioperative stroke after general surgery procedures. There has been much speculation about the importance of carotid bruits in the pathogenesis of postoperative stroke.^{1,7} Some studies have reported an increased incidence of perioperative stroke with the presence of a preoperative carotid bruit or a history of transient ischemic attacks (TIAs).

The purpose of this study was to identify the preoperative, intraoperative, and postoperative factors associated with perioperative strokes after general surgical procedures.

PATIENTS AND METHODS

The records of all general, head and neck, plastic, and vascular surgery patients who sustained a perioperative stroke at the Long Island Jewish Medical Center were retrospectively reviewed for a five-year period of time. From a total of 24,641 surgical procedures, 19 patients (0.08%) suffered perioperative strokes. Patients were identified by morbidity and mortality records, represents the most accurate surveillance of postoperative problems at our institution. Patients undergoing carotid endarterectomy were specifically excluded. All strokes were confirmed by neurological consultation and positive computed tomography (CT) scans.

These 19 patients were compared to a group of 19 patients matched for age and procedure operated upon during the same five-year period of time. The charts of both groups (38 patients) were analyzed for associated medical diseases (hypertension, heart disease, diabetes mellitus); presence of a carotid bruit; earlier neurological symptoms (TIAs, cerebrovascular attacks); laboratory values (hematocrit, platelet count, prothrombin and partial thromboplastin times); electrocardiogram; intraoperative events (blood pressure range, heart rate and rhythm, length of anesthesia, and estimated blood loss); events preceding CVA and time of CVA in relation to surgery; medications including anticoagulants; CT findings, and social history (cigarette smoking) (Table I).

Long-term follow-up was obtained by direct conversation with the patient or a close relative, and by physical and mental status evaluation. Patients were assigned to one of four categories: complete recovery, 90% recovery, partial recovery, and completely disabled. Fisher's exact test and the paired *t*-test were used to determine if a significant difference existed between the groups when comparing them for different factors.

RESULTS

Of the 24,641 patients, 19 (0.08%) had a perioperative CVA after a surgical procedure. There were eleven males and eight females. Twenty-six percent of the patients had primary peripheral vascular procedures. The age of the patients ranged from 37-90 years (mean 67 years); 74% were aged 65 years or older. The timing of the stroke in relation to surgery occurred within 24 hours in 53% of patients (*n* = 10); within one to seven days postoperatively in 26% of patients (*n* = 5) and after seven days in 21% of patients (*n* = 4). Only one patient had an intra-operative CVA attributed to hypotension. CT scans revealed bland infarctions in all but one patient who had an intracerebral hemorrhage. Duplex scans post-stroke revealed significant carotid disease on the appropriate side in only two patients.

The postoperative course for all patients with a perioperative CVA was carefully reviewed to identify the following specific precipitating factors: hypertension (*n* = 1), myocardial infarction with hypotension (*n* = 1), subacute bacterial endocarditis (*n* = 1), carotid stenosis (*n* = 2), and atrial fibrillation (*n* = 6). No cause was identified in seven patients. In the one patient who was hypertensive (220/110) for five minutes immediately post-op, the CT scan revealed an intracerebral hemorrhage. Interestingly, only one patient had documented carotid bruits before surgery. This patient had bilateral bruits and a history of a left CVA and left carotid endarterectomy. On the fourth postoperative day, the patient had a right CVA. Another patient had no carotid bruits but began to have TIAs on the tenth postoperative day, and subsequently had a CVA on the 22nd day after surgery.

Six patients (32%) had atrial fibrillation on their electrocardiograms preceding their CVA. In four patients, the fibrillation was present before surgery and in two patients, the

TABLE I. Patients With Perioperative Stroke and Controls by Age, Sex, and Procedures Performed

Stroke Patients			Controls		
Procedure	Age	Sex	Procedure	Age	Sex
Incisional hernia	52	F	Incisional hernia	52	F
Vagotomy/bilroth II	68	F	Vagotomy/bilroth II	68	F
Esophagogastrectomy	65	F	Esophagogastrectomy	65	F
Takedown fistula/subtotal colectomy	37	M	Total proctocolectomy	39	M
Cholecystectomy/small bowel resection	79	M	Cholecystectomy/Common duct exploration	81	M
Aortobifemoral bypass	61	F	Aortobifemoral bypass	51	F
Aortic endarterectomy	65	F	Aortobifemoral bypass	62	F
Rectus flap closure of chest wound	70	M	Rectus flap closure of groin wound	69	M
Right hemicolectomy	80	M	Right hemicolectomy	76	M
Cholecystectomy/common duct exploration	76	M	Cholecystectomy/common duct exploration	68	F
Aortobiiliac bypass	62	M	Aortobiiliac bypass	59	M
Femoral-peroneal bypass	88	F	Femoral-tibial bypass	89	F
Cholecystectomy	90	F	Cholecystectomy	79	F
Sigmoid resection	66	F	Sigmoid resection	64	F
Femoral-popliteal bypass	70	F	Femoral-popliteal bypass	72	F
Whipple procedure	69	F	Whipple procedure	73	F
Exploratory laparotomy (perforated ulcer)	44	M	Exploratory laparotomy (perforated ulcer)	54	M

abnormal rhythm developed postoperatively. In the remaining seven patients (37%), no precipitating factors were noted.

The preoperative data of each patient were analyzed for risk factors for the development of perioperative CVA and compared with the same preoperative data of the control group (Table II). Four risk factors were found to be significantly different between the two groups: hypertension, smoking, early neurological symptoms, and abnormal rhythm on electrocardiogram. Earlier neurological symptoms included optic migraine, TIA, and CVA. A history of diabetes, intraoperative blood loss, and the length of anesthesia were not significantly different between the groups.

The in-hospital mortality rate was 26%. Four patients died of a cardiac arrest (one within 24 hours after the CVA, and the others at 46, and 13 days after the CVA, respectively). The fifth patient succumbed to pneumonia and sepsis nine days after the CVA. Complications from the stroke such as obtundation, prolonged ventilating support, pneumonia, and multisystem failure lead to death in three of the five patients. The long-term follow-up is listed in Table III. Four patients were lost to follow-up.

DISCUSSION

The four significant preoperative risk factors identified in this study for the development of a perioperative CVA include an abnormal rhythm on electrocardiogram, earlier neurological symptoms, hypertension and a history of smoking. All of these factors suggest that diffuse atherosclerosis is common in these patients.

Only one patient of the 19 had a preoperative carotid bruit, suggesting that cervical bruit is an unreliable predictor of stroke risk. Several prospective and retrospective studies^{1,5,7} have failed to demonstrate a correlation between carotid bruits and incidence of perioperative stroke. At present, ours and others data indicate that an symptomatic bruit is not a significant risk factor for the development of a perioperative stroke.^{9,10,11,12} However, one must be cautious in interpreting our data given the limitations of negative findings with a small sample size ($n = 19$).

Although an asymptomatic carotid bruit is an unreliable predictor of perioperative stroke risk, our data suggest that previous neurological symptoms, with or without a bruit, is a significant risk factor for perioperative stroke. Seven of the stroke patients (37%) had a history of neurological symptoms, and one patient developed TIAs postoperatively to subsequently suffer a CVA. Knapp⁸ reported a four-fold increase in the incidence of postoperative CVA in patients with a previous history of CVA and Landercasper¹³ re-

TABLE III. Follow-up of Patients with Perioperative Stroke After General Surgical Procedures

	<i>n</i>	Percentage
Perioperative death	5	(26)
Death within 12 months	4	(21)
Completely disabled	1	(5)
Partial recovery	1	(5)
90% recovery	2	(11)
Complete recovery	2	(11)
Lost to follow-up	4	(21)

ported a perioperative stroke risk of 2.9% for patients with a past history of stroke. On the basis of our data and these studies, we recommend a complete work-up for the patient with a history of neurologic symptoms before his or her surgical procedure. This should include a scan and duplex scan of the carotid arteries. Consideration might then be given to carotid endarterectomy if a stenosis of greater than 70% is identified. However, prophylactic carotid endarterectomy before general surgical procedures remains controversial.

Six patients suffering a postoperative CVA had an abnormal rhythm on their electrocardiogram, mainly atrial fibrillation. Most cardiac arrhythmias cause a reduction in the cerebral blood flow and an increase in the arterial resistance.¹⁴ Rapid ventricular rates in atrial fibrillation cause an average reduction of cerebral blood flow by 23%. In addition, cerebral angiospasm occurs during the cardiac arrhythmias, and its effect lasts for as long as one hour after conversion of the arrhythmia. If cerebral artery narrowing is present, it is possible that the collateral circulation to a vital area of the brain will fail because of the reduced head of pressure and blood flow. Reed¹⁵ in a study of 290 patients with cardiac dysrhythmias of the type associated with significant reduction in cardiac output reported only a 1% incidence of focal neurologic symptoms or signs. This supports a thromboembolic mechanism for the development of a CVA and not merely a reduction in blood flow.

The reported overall mortality for the first occurrence of strokes range from 15%–46%.^{12,16} The in-hospital mortality rate in this study was 26% all within two weeks. In addition to the high perioperative mortality, the long-term prognosis is poor. In follow-up, four patients died within a mean time of 12 months and of those patients available for follow-up ($n = 15$), only three (27%) recovered enough to live a normal life.

TABLE II. Significant Risk Factors for Stroke in Patients With Cerebrovascular Accidents and Controls

	CVA (<i>n</i> = 19)	Controls (<i>n</i> = 19)	<i>P</i> Value*
Male:Female	11:8	14:5	NS
Carotid bruits	5.2%	0	NS
HX of heart disease	42%	26%	NS
HX of diabetes	26%	16%	NS
HX of smoking	58%	37%	0.09
HX of hypertension	68%	31%	0.025
Prior neurological symptoms	37%	5.2%	0.02
Abnormal rhythm on cardiogram	32%	5.2%	0.04
Mortality	26%	5.2%	0.08
Estimated blood loss	462 cc	492 cc	NS†
*Number of cardiac medications	1.58	1.0	.19‡

*Fisher's exact test.

†Paired T-test.

‡Digoxin, methyl dopa, propranolol, dipyridamole, aspirin, verapamil, metoprolol, labetalol, atenolol, captopril, furosemide, nifedipine, nitroglycerin ointment.

A history of hypertension, history of smoking, previous neurological symptoms, and abnormal cardiac rhythms were identified as significant risk factors for the development of perioperative stroke. Although, the exact mechanism of perioperative stroke remains unclear, its association with abnormal cardiograms, lack of association with carotid bruits, and lack of intracerebral hemorrhage suggest that emboli from the heart was the major cause in most patients. Unfortunately, cardiac emboli are probably unpreventable unless all of the patients are anticoagulated. In elderly patients on anticoagulants for cardiac arrhythmias, we would recommend perioperative heparinization, including full-dose heparin up to six hours before the surgical procedure and then resumption of full dose heparin 24 hours after the operative procedure. This may afford these patients on chronic anticoagulation some protection through the perioperative period. In elderly patients with significant cardiac arrhythmias not previously on anti-coagulants, consideration might be given to placing them on perioperative heparin up to six hours before the procedure and then restarting the heparin 24 hours after the operative procedure with continuation of full dose heparin for 48 to 72 hours after the general surgical procedure.

In the small group of patients who have had earlier neurological symptoms, some further preoperative work-up might be beneficial. Although the data were unclear, a patient with previous neurological symptoms with a carotid lesion in the territory of his previous stroke or neurological symptoms might benefit from a carotid endarterectomy before the general surgical procedure. In this small subgroup of patients, further preoperative work-up would include scans and duplex scanning in an attempt to identify a correctable carotid lesion. If a correctable lesion is not identified, consideration might also be given to the use of perioperative heparinization in these patients.

It should be emphasized that the treatment options suggested above are speculative and the view of authors. A randomized prospective study of patients with these risks factors would be required to adequately decide the best therapeutic options.

REFERENCES

1. Turnipseed WD, Berkoff HA, Belzer FO: Postoperative stroke in cardiac and peripheral vascular disease. *Ann Surg* 1980; 192:365-368.
2. Hart R, Hindman B: Mechanisms of perioperative cerebral infarction. *Stroke* 1982; 13:766-773.
3. Hang CA, Dale WA: Major surgery in old people. *Arch Surg* 1952; 64: 421-437.
4. Carney WI, Stewart WB, DePinto DJ, et al: Carotid bruit as a risk factor in aortoiliac reconstruction. *Surg* 1977; 81:567-570.
5. Treiman RL, Foran RF, Cohen JL, et al: Carotid bruit: a follow-up report on its significance in patients undergoing an abdominal aortic operation. *Arch Surg* 1979; 114:1138-1140.
6. Larsen SF, Zaric D, Boysen G: Postoperative cerebrovascular accidents in general surgery. *Acta Anaesthesiol Scand* 1988; 32:698-701.
7. Ropper AH, Wechsler LR, Wilson LS: Carotid bruit and the risk of stroke in elective surgery. *New Engl J Med* 1982; 307:1388-1390.
8. Knapp RB, Topkins MJ, Artusio JF: The cerebrovascular accident and coronary occlusion in anesthesia. *JAMA* 1962; 182:332-334.
9. Gutierrez IZ, Barone DL, Makula PA, et al: The risk of perioperative stroke in patients with asymptomatic carotid bruits undergoing peripheral vascular surgery. *Amer Surg* 1987; 53:487-489.
10. Furlan AJ: Risk of stroke from carotid bruits. *New Engl J Med* 1989; 320:936-937.
11. Heyman A, Wilkinson WE, Heyden S, et al: Risk of stroke in asymptomatic persons with cervical arterial bruits: a population study in Evans County, Georgia. *New Engl J Med* 1980; 302:838-841.
12. Wolf PA, Kannel WB, Sorlie P, et al: Asymptomatic carotid bruit and risk of stroke: the Framingham study. *JAMA* 1981; 245:1442-1445.
13. Landercasper J, Merz BJ, Cogbill TH, et al: Perioperative stroke risk in 173 consecutive patients with a past history of stroke. *Arch Surg* 1990; 125:986-989.
14. Corday E, Irving DW: Effect of cardiac arrhythmias on the cerebral circulation. *Am J Cardiol* 1960; 6:803-807.
15. Reed RL, Siekert RG, Merideth J: Rarity of transient focal cerebral ischemia in cardiac dysrhythmia. *JAMA* 1973; 223:893-895.
16. Sacco RL, Wolf PA, Kannel WB, et al: Survival and recurrence following stroke: the Framingham study. *Stroke* 1982; 13:290-295.

Compliance with New York State's do-not-resuscitate law at Memorial Sloan-Kettering Cancer Center

A review of patient deaths

ROBERT I. MISBIN, MD; DANIEL O' HARE, PhD; MARGUERITE S. LEDERBERG, MD; JIMMIE C. HOLLAND, MD

ABSTRACT. We reviewed the case records of 141 patients (134 with cancer and seven with acquired immunodeficiency syndrome) who died at Memorial Sloan-Kettering Cancer Center between July 11 and September 19, 1991. Do-not-resuscitate orders had been written on 115 (85.8%) of the patients with cancer and all of the patients with acquired immunodeficiency syndrome. The do-not-resuscitate orders appeared to be valid, in that evidence of informed consent was documented in all but two of the cases. Six additional patients who died had family consent not to resuscitate, although no do-not-resuscitate orders were written. Two other patients died unexpectedly. The

remaining 11 patients all received aggressive attempts at resuscitation, which were felt to be medically appropriate in all but two cases. The interval between the do-not-resuscitate order and death was between zero and 60 days, with an average of 8.4 days and a median of 6 days; it exceeded 20 days in 14 cases. We attribute the high degree of compliance with the New York State do-not-resuscitate law observed in this study to an intensive program of consultation and education begun in 1987 by the Ethics Committee of Memorial Sloan-Kettering Cancer Center.

(NY State J Med 1993; 93:165-168)

From the Department of Psychiatry, Memorial Sloan-Kettering Cancer Center, New York, NY.

Address correspondence to Dr Misbin, Department of Medicine, JHMC Box J226, University of Florida College of Medicine, Gainesville, FL 32610.

On April 1, 1988, New York became the first state to legislate conditions under which physicians could withhold attempts at resuscitation from patients who experienced cardiopulmonary arrest. Under the law, consent for cardio-

pulmonary resuscitation (CPR) is presumed unless the patient or an appropriate surrogate agrees to a do-not-resuscitate (DNR) order. Therefore, patients who die in a New York hospital should either have had a DNR order entered in their medical record or have received an aggressive, albeit unsuccessful, attempt at resuscitation. Although physicians are not required to attempt resuscitation when they consider it to be medically futile, the law restricts the definition of futility to cases in "which attempts at resuscitation would likely be unsuccessful or would lead to repeated arrests, with death ensuing over a short period of time."¹

Some physicians have complained that the presumption in favor of resuscitation, plus the complexity of obtaining a DNR order, would lead to some patients being resuscitated inappropriately or to "show codes/slow codes," in which an attempt at resuscitation is half-hearted and hides the true intention, which is to let the patient die.^{2,3} However, data from hospitals in Westchester^{4,5} and Rochester⁶ have failed to show any major effect of the legislation on previously existing hospital policy. Kamer et al^{4,5} from the Westchester County Medical Center suggest that the major effect of the legislation has been to facilitate discussions of DNR orders between physicians and patients/families.

Memorial Sloan-Kettering Cancer Center (MSKCC) comprises Memorial Hospital, a 565-bed tertiary care hospital for cancer, and the Sloan-Kettering Institute, which has an international reputation for cancer research. MSKCC is known for both its basic cancer research and early application of findings to clinical care.

Patients who come to Memorial Hospital seeking treatment using new research findings often have been told that conventional therapies will be ineffective in their cases. Depending on the diagnosis and stage of disease, patients may be asked to participate in clinical trials in which standard treatment is compared to investigational treatment, or to receive a treatment that has not yet been shown to be effective. Because the nature of the institution is to foster aggressive treatment, we hypothesized that discussion of terminal care issues might be more difficult at Memorial than it is in other hospitals, and that the need to comply with the New York State DNR law would create additional problems.

METHODS

One hundred and forty-four patients died at Memorial Hospital between July 11, 1991, and September 19, 1991. We were able to review the records of 103 patients soon after they died and before their charts were sent to the medical records department.

Thirty-eight additional charts were retrieved from the medical records department and reviewed at a later date. The records of the remaining three patients could not be located.

We determined whether the patient had a DNR order at the time of death, and if so, on what basis the DNR order had been made. We looked specifically for cases in which the attending physician might have written a DNR order without having obtained consent from the patient or appropriate surrogate. For patients who died without a DNR order, we noted if an aggressive attempt was made at resuscitation, and whether progress notes indicated if members of the health-care team agreed that resuscitation was appropriate.

Particular attention was paid to discrepancies between notes written by physicians and notes written by nurses and social workers. Evidence of disagreement among health-care provid-

ers about the appropriateness of resuscitation or about the capacity of the patient to give consent was also sought.

RESULTS

Of the 141 patients whose medical records were reviewed, 134 patients died of cancer and seven patients died of acquired immunodeficiency syndrome (AIDS). As shown in Table I, 122 patients (86.5%) died with a DNR order. This group included 115 of the cancer patients and all seven of the AIDS patients. Of the patients who died without a DNR order, two were found dead unexpectedly. Six patients died with family consent not to use CPR but without a written DNR order. Eleven additional patients received aggressive but unsuccessful attempts at resuscitation. In all but two cases, the medical record reflected agreement between health-care providers and the patient and/or family that resuscitation was warranted. In one of those two cases, the attending physician wrote in the chart that resuscitation was attempted only to satisfy the requirements of New York State law and that, in his judgment, resuscitation was medically inappropriate. This case was that of a woman aged 81 years, who had a bowel obstruction due to an unresectable ovarian carcinoma. She had been treated with *cis*-platinum and total parenteral nutrition but had not responded well. She had a history of congestive heart failure, which had worsened during her 40-day hospital stay. A DNR order was discussed with the patient two days before her death, but she refused to give consent. The second case was a 67-year-old man with ascites and liver failure due to metastatic colon cancer. The family refused to agree to a DNR order because they wanted the patient to receive more chemotherapy. He died the day after the DNR discussion and could not be successfully resuscitated.

Table II shows the basis on which the DNR orders were written. In 108 cases (88.5%), the DNR order was accompanied by completion of one of the six standard consent forms recommended by the New York State Department of Health. In 13 more cases, the standard DNR forms were not used, but sufficient information was obtained from the medical record to allow classification into one of the six categories. In one additional case, the DNR order was not accompanied by any explanatory note. As shown in Table II, 53.3% of DNR orders were written on the basis of the consent of a surrogate for a patient who had lost decision-making capacity. In 33 cases (27.1%), the patients themselves had consented to the order. However, in one of these cases, the record showed that the patient was being treated for delirium at the time consent was said to have been given, and no one witnessed the consent other than the physician who wrote the order. The family was noted to have been dissatisfied with the care that the patient was receiving and had requested a second opinion regarding his medical treatment. They were not consulted about resuscitation.

TABLE I. Do Not Resuscitate Order Status of Patients at Memorial Sloan-Kettering Cancer Center, July 11, 1991–September 19, 1991

	No.	%
DNR order written	122	86.5
No DNR order written	19	13.5
Unsuccessful cardiopulmonary resuscitation	11	7.8
Died with family consent not to resuscitate but no DNR order written	6	4.3
Unexpectedly found dead in bed	2	1.4
Total	141	100.0

TABLE II. Basis for the Do Not Resuscitate Order

Basis for DNR Order*	Form†	No Form†	Total	Percentage
1. Patient with capacity	32	1	33	27.1
2. Therapeutic exception	7	0	7	5.7
3. Previous DNR	3	4	7	5.7
4. Patient without capacity with a surrogate	58	7	65	53.3
5. Patient without capacity without a surrogate	0	0	0	0.0
6. Minor	8	1	9	7.4
7. Unspecified	0	1	1	0.8
Total	108	14	122	100.0

*Basis for DNR order refers to the consent forms of the New York State Department of Health.

†Form/No form refers to whether the consent form was signed or not.

As shown in Figure 1, there was wide variability in the number of days between the writing of the DNR order and the patient's death. In 12 cases, the DNR order was written on the day the patient died.

In contrast, there was one case of a patient with AIDS dementia for whom the patient's brother consented to a DNR order 60 days before the patient's death. There were 13 cases in which DNR orders were written more than 20 days before the patient's death.

DISCUSSION

In spite of the increase in paperwork and complexity brought about by the New York State DNR law, and the frustration it initially engendered among many physicians and hospital administrators, the results of this study show excellent compliance at a cancer research hospital in which the frequency of deaths probably far exceeds that in general hospitals. There was a DNR order for 85.4% of the patients who died, and in only two instances was there evidence that the physician who wrote the order had not obtained valid informed consent. In an additional 4.3% of deaths, the family agreed that no resuscitation was to be performed, but no DNR order was written. We believe that the requirement that the surrogate sign the DNR form was the reason that no formal DNR order was written in these cases. Three of these six cases involved dying children, and the notes reflected the parents' grief, even though the deaths were expected. Before the recent amendment to the DNR legislation, which permits oral consent, the hospital

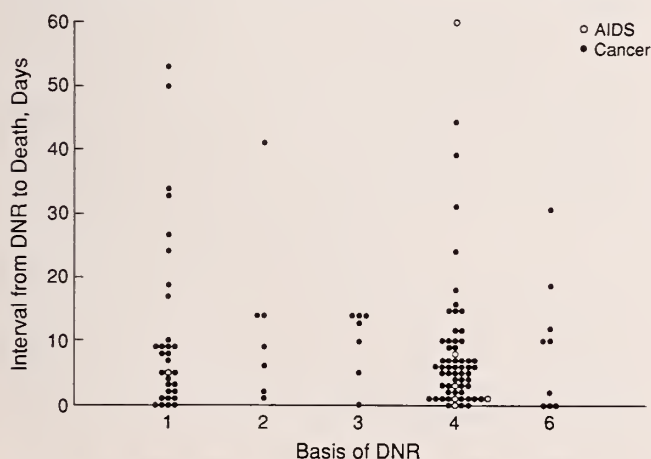


FIGURE 1. Interval between DNR order and death: Data show the number of days between the DNR order and the patient's death displayed according to the basis for the DNR order (as described in Table II).

Ethics Committee felt that an accommodation should be made for parents who, while agreeing to a DNR order for their children, were yet unable to sign the consent form. During training in DNR, the staff was encouraged to provide documentation in the progress notes of both the agreement to the order and any psychological reasons for hesitation to sign the consent. Contrary to what had been predicted,^{2,3} we found no instances of half-hearted attempts at resuscitation. However, there were two cases in which the patient or family refused to agree to a DNR order, and resuscitation was attempted even though the attending physician felt it was unwarranted.

Sulmasy et al⁷ recently reported that giving house officers a course in medical ethics results in more involvement of patients and appropriate surrogates in discussions about DNR. Likewise, we attribute the excellent compliance with the DNR law observed in the present study to an intensive educational and consultation program carried out by the MSKCC Ethics Committee. The committee was established in 1984 with a threefold mission of education of staff, consultation on policy issues, and development of a consultation advisory service for staff when conflicts or ethical dilemmas arose. The committee developed guidelines which were implemented as a hospital-wide DNR policy in 1985, and which were revised in 1988 to be consistent with the New York State DNR law. The committee was also responsible for reviewing medical records to ensure compliance. The last review, performed in June 1990, showed that 17% of patients had a DNR order. This was approximately the same as found in reviews before the DNR law.^{8,9} The present study dealt only with patient deaths. We do not have data on how many patients who have DNR orders die in the hospital versus how many are discharged. Reports from other hospitals have shown a range between 13% and 60% for the fraction of patients with DNRs orders who die while in the hospital.¹⁰⁻¹²

The high degree of compliance with the New York State DNR law observed in this study should not be taken as evidence that the law necessarily fosters good, ethical decision making. MSKCC has a highly educated patient population, which according to a recent report by Miller et al¹³ would be expected to be more likely to refuse CPR. There is also evidence that physicians find it easier to deal with resuscitation issues in patients dying of AIDS and cancer than in patients dying of other causes.¹⁴

On December 1, 1991, the federal Patient Self-Determination Act became effective, requiring that health-care facilities inform patients of their right to refuse

life-sustaining treatment and inquire if patient have executed advance directives. At the time this bill was passed by Congress, most states had already followed the example set by California in 1976 and adopted "natural death" legislation that allows previously competent patients to have life sustaining treatment withheld or withdrawn on the basis of an advance directive. Although New York never passed such legislation, the Health Care Proxy Act, which took effect January 18, 1992, allows patients to designate a proxy who is empowered to make health-care decisions on the patient's behalf, including the removal of artificial life support. In the absence of such a proxy, withdrawal of life support is difficult in New York State because of case law, which requires a standard of "clear and convincing evidence" that withdrawal of life support would have been the patient's wish. As noted by McClung and Kamer,⁵ the DNR law creates a specific exception to the "clear and convincing evidence" standard by allowing that cardiopulmonary resuscitation be withheld on the basis of the substituted judgment of an appropriate surrogate.⁵ Thus, family members of patients in New York must be informed that if they refuse to consent to a DNR order, they may find later, after the patient has suffered cardiac arrest and been placed on artificial life support, that their wishes to have life support withdrawn might not be obeyed.

In conclusion, the results of this study show that despite the confusion and criticism that was initially generated by the New York State statute, a review of 141 deaths at a major cancer research institute has demonstrated excellent compliance. This is due in large part to the results of an intensive program of staff education and individual case consultation by the institution's Ethics Committee. We suggest that hospital ethics committees can be an impor-

tant resource in resolving difficulties with implementation of the law.

REFERENCES

1. Swidler RN: The presumption of consent in New York State's do not resuscitate law. *NY State J Med* 1989; 89:69-72.
2. Prager K: Implication of New York's do not resuscitate law. [letter] *N Engl J Med* 1988; 318:1758.
3. Plowe CV: Life support and resuscitation. [letter] *N Engl J Med* 1988;318:1758.
4. Kamer RS, Dieck EM, McClung JA, et al: Effect of New York State's do not resuscitate legislation on in-hospital cardiopulmonary resuscitation practice. *Am J Med* 1990; 88:108-111.
5. McClung JA, Kamer RS: Implications of New York's do not resuscitate law. *N Engl J Med* 1990; 323:270-272.
6. Quill TE, Bennett NM: The effects of a hospital policy and state legislation on resuscitation orders for geriatric patients. *Arch Intern Med* 1992; 152:569-572.
7. Arch Intern Med 1992; 152:569-572.
8. Sulmasy DP, Geller G, Faden R, et al: The quality of mercy: caring for patients with do not resuscitate orders. *JAMA* 1992; 267:682-686.
9. O'Hare O: Impact of New York State's do not resuscitate law on clinical practice in a cancer research institution, presented at "Controversies in the Care of the Dying Patient," Orlando, FL, February 14, 1991.
10. Ethics group of Memorial Sloan Kettering Cancer Center: Impact of the New York State do not resuscitate law on clinical practice in a cancer research institution, in Misbin RI (ed): *Euthanasia. The Good of the Patient, the Good of Society*. The University Publishing Group, Frederick Maryland, pp 107-116, 1992.
11. Misbin RI: Do not resuscitate orders. *J Fla Med Assoc* 1990; 77:901-903.
12. Torian LV, Davidson EJ, Fillit HM, et al: Decisions for and against resuscitation in an acute geriatric medicine unit serving the frail elderly. *Arch Intern Med* 1992; 152:561-565.
13. Stollman CJ, Gregory JJ, Dunn D, et al: Evaluation of the do not resuscitate orders at a community hospital. *Arch Intern Med* 1992; 149:1851-1856.
14. Miller DL, Jahnigan DW, Gorbien MJ, et al: Cardiopulmonary resuscitation: how useful? Attitudes and knowledge of an elderly population. *Arch Intern Med* 1992; 152:578-582.
15. Wachslar RM, Luce JM, Hearst N, et al: Decisions about resuscitation: inequities among patients with different diseases but similar prognoses. *Ann Intern Med* 1989; 111:525-532.
16. Rouse F: Surrogate decisions in New York State on sustaining life. *Mt Sinai J Med* 1991; 58:1-4.

The use of α -blockers in the management of benign prostatic hyperplasia

FRANKLIN C. LOWE, MD, EDWARD STARK, MD

Benign prostatic hyperplasia (BPH) affects approximately 50% of men aged 60.¹ By age 80, approximately 80% will be symptomatic.² Transurethral prostatectomy (TURP) has been the standard form of therapy for the last 50 years. However, outcome research has demonstrated that results are less favorable than assumed, with higher than estimated reoperation rates and mortality.³ Therefore, it is not surprising that many different alternative strategies for the treatment of BPH have been investigated (Table I). Medical management with α -adrenergic blockade was initially promulgated by Dr Marco Caine. Since his pioneering work in this area, numerous other investigations have been undertaken in this promising area of BPH management. This article reviews the management of symptomatic BPH with α -adrenergic blockade.

RATIONALE FOR α -BLOCKADE IN BPH

BPH arises from either the transition zone or the periurethral region.⁴ McNeal⁴ has shown that most periurethral nodules are stromal in nature, whereas transition zone nodules are primarily glandular. Stromal hyperplasia is more common than glandular hyperplasia of the prostate. The normal human prostate has a stromal to epithelial ratio of 2:1. With the development of BPH, this ratio can increase to 15:1, especially in the stromal form of the fibromuscular nodule.⁵

Lepor et al⁶ found high affinity α_1 -adrenergic, α_2 -adrenergic and muscarinic-cholinergic (Mch) receptors in the human prostate. The Mch receptor density was two-fold greater than the α -adrenergic receptors. The density of α_1 - and α_2 -adrenergic receptor sites was equivalent. The contractile response of the α_1 -adrenergic receptor, however, was much greater than either the α_2 -adrenergic or Mch receptor. This indicated that smooth muscle (~40% of the prostate adenoma) contractions are mediated by the α_1 -receptor. The Mch receptor is primarily associated with the glandular component of the prostate and does not mediate smooth muscle contraction. The α_2 -adrenergic receptor may act presynaptically to inhibit norepinephrine release, but its role is still unclear.

Caine⁷ postulated that there are two components, mechanical and dynamic, that account for the urethral obstruction in BPH. The mechanical component is related to the actual physical obstruction caused by the enlarged adenoma. The dynamic component results from the sympathetic tone of the gland mediated by α_1 -adrenergic recep-

tors. Although these α_1 -receptors are abundant at the bladder neck, prostate capsule, and prostatic stroma, they are sparse in the bladder body.⁸ Thus, α_1 -blockade results in a decrease in outlet resistance without a measurable effect on detrusor smooth muscle contractility. This underlies the rationale for the use of selective α_1 -blockade therapy for the treatment of BPH.

Many different α -blockers have been evaluated for the treatment of symptomatic BPH (Table II). The three most commonly studied drugs have been phenoxybenzamine, prazosin, and terazosin. Phenoxybenzamine, a non-selective α_1 - and α_2 -blocker was the earliest and most widely studied α -blocker. It was used sporadically clinically but fell out of favor due to frequent adverse reactions. Prazosin, a selective α_1 -blocker, with fewer adverse reactions than phenoxybenzamine subsequently was evaluated and sporadically used clinically. However, terazosin, a long-acting α_1 -blocker, with its long half-life that provides for once daily dosing has gained wider acceptance and usage than twice a day prazosin. The clinical trials, evaluating these three α -blockers are reviewed here within.

PHENOXYBENZAMINE

Boreham et al⁹ placed 30 men with BPH on phenoxybenzamine 10 mg twice daily for seven days. Three patients withdrew secondary to adverse reactions. Eighteen patients reported their voiding symptoms as improved and seventeen markedly so. A total of 19 patients had side effects, most common being dizziness and lethargy. This study confirmed both the efficacy as well as the high adverse event profile of phenoxybenzamine.

Caine et al¹⁰ evaluated 50 patients with BPH in a double-blind placebo controlled study. Twenty-four patients received phenoxybenzamine 10 mg orally twice daily and the remainder received placebo. One patient from the placebo group withdrew due to a stroke. Re-examination of patients after 14 days of therapy showed a significant improvement in peak and mean urinary flow rates as compared to the placebo group. There was no significant difference between the two groups with regards to post void residual urine. Both diurnal and nocturnal frequency were also significantly decreased. The most common side effects were dizziness and tiredness but did not require cessation of medication.

Gerstenberg et al¹¹ reported on nine patients with BPH who were evaluated after four weeks of therapy on 15 mg of phenoxybenzamine daily. There was a statistically significant decrease in urethral resistance, post void residual, opening pressure, maximum micturition pressure, and detrusor contraction pressure. Diurnal and nocturnal fre-

From the Department of Urology, St Luke's-Roosevelt Hospital Center, New York City.

Address correspondence to Dr Lowe, Associate Director of Urology, St Luke's-Roosevelt Hospital Center, 425 W 59th St, New York, NY 10019.

TABLE I. Alternative Strategies for the Treatment of Benign Prostatic Hyperplasia

Observation
Surgical/Interventional
Open prostatectomy
Transurethral prostatectomy
Transurethral incision of prostate or bladder neck
Balloon dilatation
Prostatic urethral stent
Microwave hyperthermia
Laser prostatectomy or incision
Orchiectomy
Pharmacologic
Estrogen
LHRH agonists
Antiandrogens
5 α -reductase inhibitors
Aromatase inhibitors
α -adrenergic blockers

quency also decreased significantly. A statistically significant increase was found in first sensation to void, bladder capacity, and maximal and average flow rates. A report of adverse reactions was not mentioned.

Caine et al¹² reported a retrospective study of the largest series with 200 patients having been treated with phenoxybenzamine. Patient dosages varied but the usual dosage taken by 98% of the patients was either one or two 10 mg capsules a day. Obstructive symptoms improved in 78.7% of patients. Improvement in nocturnal and diurnal frequency was found in 75.9% and 66.9% of subjects, respectively. In the 102 patients who had pre and post treatment uroflow recordings, peak urinary flow rates doubled in 46% and were increased by between 50%–100% for another 26% of the patients. In 90% of patients side effects were absent or tolerable. Most common adverse events were dizziness, weakness, or palpitations.

Abrams et al¹³ evaluated the effectiveness of phenoxybenzamine in a two part study. Phase one was a four week double-blind placebo trial of 41 patients on 10 mg twice daily. Phase two was a four week open trial of twenty patients on the same dose. Only patients in the double-blind phase were evaluated for symptoms and side effects. Symptoms of hesitancy and slow stream were significantly improved in the phenoxybenzamine group. The symptoms of frequency, nocturia, urgency and incontinence were not significantly changed. There was also a significant decrease in residual urine and a significant increase in maximum flow rate. Side effects mainly consisted of dizziness and postural hypotension requiring withdrawal of three patients from phase two but none from phase one.

TABLE II. α -Blockers Used to Treat Benign Prostatic Hyperplasia

Non-selective α -blockers
Phenoxybenzamine
Thymoxamine
Selective α -blockers
Prazosin
Nicergoline
Alfuzosin
YM-12617
Selective long-acting α -1 blockers
Terazosin
Doxazosin

Brooks et al¹⁴ randomly divided 28 patients with BPH in two groups. One group took 10 mg of phenoxybenzamine at night while the other received one tablet of vitamin B. The patients were re-examined at 30 days to evaluate urine flow, post-void residual and urethral pressure profile. In the phenoxybenzamine group two patients dropped out secondary to orthostatic hypotension and one patient in the placebo group because of urinary retention. On the basis of 15 patients taking active drug and nine on placebo, their findings showed no statistically significant difference with regards to post void residual, peak and mean urinary flow rates or urethral pressure profiles. The failure to achieve efficacy in this study, could have been related to the low dose of phenoxybenzamine administered.

Griffiths et al¹⁵ reported on a four-week, double-blind, placebo-controlled trial. Four patients received 20 mg daily of phenoxybenzamine, six patients received 10 mg per day and six took placebo. There was a statistically significant increase in adverse reactions compared with the placebo group. All but three patients on active drug complained of impotence, dizziness, or nasal stuffiness. No significant difference between placebo and active drug were observed for prostate volume, maximum flow rate, or residual urine. Statistical significance on active drug was found only for a decrease in nocturia and prostatic plateau pressure.

Ferrie et al¹⁶ evaluated 15 patients with BPH in a double-blind study using phenoxybenzamine 10 mg per day for five weeks. Six patients were withdrawn secondary to non-compliance and two were withdrawn because of adverse reactions. There was no significant difference between active drug and placebo regarding peak urinary flow rates, voided volume, residual urine, day frequency and nocturia. Hesitancy, urgency and slow stream were all significantly improved with phenoxybenzamine compared with placebo. Side effects occurred in 47.6% on active drug and 22.2% on placebo. Thus, almost all the above studies demonstrated a positive affect of α -adrenergic blockade for various subjective and objective parameters for the evaluation of patients with BPH. None of the studies was "long-term;" four to six weeks of therapy was the norm. Phenoxybenzamine was effective short-term therapy for symptomatic BPH but was not clinically very useful because of its high adverse event profile.

PRazosin

Prazosin, a selective α_1 -adrenergic blocker, was subsequently evaluated. Because of phenoxybenzamine's poor adverse event profile, it was postulated that the selective α -blockers would be better tolerated since only α_1 -adrenoreceptors would be blocked.

Hedlund et al¹⁷ reported on a double-blind crossover study evaluating 20 men with BPH. The patients were titrated to either 2 mg twice daily of prazosin or placebo for four weeks. After two weeks of therapy a crossover to the other therapy was undertaken. Post void residual and objective symptoms decreased significantly on prazosin while maximum and average urinary flow rates improved significantly. Bladder capacity, first urge to void, irritative symptoms, voiding pressure parameters and detrusor instability showed no significant change from placebo. No significant side effects were noted.

Martorana et al¹⁸ studied 18 patients with BPH in a double-blind, placebo-controlled study of prazosin 2 mg twice daily for two weeks. There was significant improvement in maximum urinary flow rate, clinical symptoms, and

cystometric parameters. Intraurethral pressure, however, was not significantly changed; again, no side effects were observed.

Kirby et al¹⁹ reported the largest series of patients with prazosin. Eighty men with BPH were in a double-blind, placebo-controlled study of prazosin titrated to 2 mg twice daily for four weeks. There were no side effects in the prazosin group; however, 25 patients withdrew mainly due to poor compliance. Thus, 28 patients in the prazosin group, and 27 in the placebo group were evaluable. Prazosin demonstrated statistically significant increases in peak flow rate, but no significant reduction in maximum voiding pressure. There was no significant difference in residual urine; however, urinary frequency was significantly reduced.

Nakamura et al²⁰ studied the effects of prazosin on the urethral pressure profile (UPP) in 14 patients with BPH. Five patients received 1 mg, while nine patients received 2 mg of prazosin. The control UPP was measured two days or more before treatment, while the post treatment measurements were made one hour after taking prazosin. The 1 mg dose showed no significant change with regards to continence zone length, functional profile length, maximum urethral closing pressure, or prostatic peak pressure. The 2 mg dose demonstrated a significant decrease in all of the above parameters except for maximal urethral closing pressure. There was no significant decrease in blood pressure with the 1 mg dose, whereas the 2 mg dose had a significant decrease in systolic blood pressure only.

Yamaguchi et al²¹ compared 77 patients on prazosin 1 mg orally three times a day to 79 patients taking the medication paraprost in a double-blind placebo controlled setting over three weeks. Paraprost, which is a widely used over-the-counter medication, contains 265 mg of L-glutamic acid, 100 mg of L-alanine, and 45 mg of aminoacetic acid. Subjective symptoms were improved in both groups, with the prazosin group showing higher improvement rates in all categories except for sensation of residual urine. However, there was no significant difference between the two medications with regards to subjective symptoms except for prolonged voiding at week two. Both medications significantly decreased day and night frequency and residual urine, but there was no significant difference between the two. The standard dose for prazosin is 2 mg twice daily; therefore, the lower dosage used in this study might account partially for the relatively small response noted. However, average and mean flow rates were significantly improved with prazosin but not with paraprost. Side effects occurred in 1.1% of patients treated with prazosin and 5.3% with paraprost.

Chapple et al²² in a double-blind, placebo-controlled, study titrated patients with BPH to prazosin 2 mg twice daily for 12 weeks. There was a total of 58 patients in the study initially, but only 22 on prazosin and 24 on placebo finished. A total of eight patients withdrew secondary to side effects, five on prazosin, and three on placebo. Maximum urinary flow rates increased with prazosin but not significantly. Maximum micturition pressure and voiding pressure at peak flow both were decreased significantly compared with placebo. There was a positive tendency toward increased volume at first unstable contraction and a reduced maximum pressure rise during filling and filling pressure, but none of these were statistically significant. No significant changes in symptoms were observed for frequency of micturition, nocturia, urgency, urge inconti-

nence, quality of urinary stream or hesitancy. Headache and dizziness were the two most common side effects.

Aokie et al²³ titrated 40 patients with BPH to a maximal daily dose of 4.5 mg of prazosin. At the end of four weeks, nine patients were receiving 1.5 mg/day, 26 were receiving 3.0 mg/day and five were receiving 4.5 mg/day. A statistically significant decrease in symptoms was observed for day and night frequency compared to pre-treatment values. The maximum and average urinary flow rates improved by 61% and 22%, respectively. Of the 40 patients, 25 (63%) were rated as much improved or improved. Only one patient developed dizziness. The above studies with prazosin have demonstrated its better adverse event profile compared with phenoxybenzamine. It too was never studied as a long-term medication.

TERAZOSIN

In an attempt to find a clinically useful therapy with high compliance, terazosin, a long active once-a-day selective α -blocker has recently been studied widely. Dunzendorfer et al²⁴ reported on a two-part study involving 15 patients with BPH. The first part involved a four-week, single-blind placebo lead-in and the second a six-month, single-blind treatment period. The subjects were titrated up to a dose of 10 mg daily. The data reported were for four months of treatment. Mean and peak urinary flow rates increased significantly. Obstructive symptom scores also improved. No patients terminated the study early due to adverse reactions.

Lepor et al²⁵ evaluated 28 patients with BPH titrated to 5 mg daily over a one-month period. Six patients did not complete the study: five due to side effects and one due to poor compliance. At the 5 mg dose, peak and mean urinary flow rates increased by 63% and 61%, respectively. Mean obstructive and irritative symptom scores decreased 62% and 33%, respectively. These were all statistically significant. Sixty-one percent of the patients indicated that their voiding symptoms were markedly improved on 5 mg, and 28% slightly improved. Overall, the mean systolic blood pressure increased by 3% and the diastolic pressure decreased by 1%. It was also concluded that urodynamic evaluation and the degree of symptomatology were unrelated to predicting the clinical efficacy of terazosin.

Fabricius et al²⁶ in a placebo-controlled, double-blind study randomized 57 patients with BPH. The study involved a four-week, placebo lead-in and a 24-week treatment period (single blind). The dose of terazosin was titrated to 10 mg daily. Thirty patients who responded to terazosin in the single-blind study were randomly assigned to placebo or terazosin in the 12-week, double-blind phase. Statistically significant improvement in peak and mean urinary flow rates and decrease in residual urine were observed. Improvements were also seen in obstructive and irritative symptom scores and physician global assessment during the single blind treatment. During the double-blind phase all these variables were sustained in the terazosin group but not in the placebo group. Most frequent adverse events were headache, asthenia, and hypotension for a total of 30%. None of these necessitated dose reduction or discontinuation of the drug.

Lepor et al²⁷ titrated 45 men with BPH to 5 mg daily for one month. Five patients were excluded secondary to adverse reactions and 87% completed the dose titration. Mean systolic and diastolic blood pressure were not altered significantly by terazosin. Mean and peak urinary flow rates

increased by 42% and 48% respectively ($p < 0.001$). Mean obstructive and irritative scores improved by 63% and 35%, respectively ($p < 0.001$). Sixty-seven percent of the patients enrolled rated the symptomatic improvement as marked, slight in 24% and unchanged in 9%. Improvement in urinary flow rate and mean obstructive symptom score, however, did not reach maximal improvement at a dose of 5 mg. Adverse reactions occurred in eleven patients with erectile dysfunction and tiredness being the most common.

Lepor et al²⁸ reported on four studies evaluating the efficacy of terazosin in men with BPH. The first study, M87-004, involved 14 patients in a single-blind study. It had two parts, a four-week, single-blind lead-in and then a four-to ten-week, single-blind treatment period. Patients were titrated to a maximum of 20 mg or until a therapeutic response was seen. No patients were terminated secondary to adverse events. The second study, M87-006, was a multicenter, long-term, single-blind study that involved 47 men in a three-part treatment period. First, was a four-week, placebo lead-in followed by an eight-week forced titration period. Finally, there was a six-month maintenance period. A maximum dose titration of 10 mg of terazosin was used. Nineteen patients did not complete the study: eight because of adverse events, three because of worsening BPH, one because of low blood pressure and seven for other reasons. The third study, M87-013, involved 57 patients in a phase III study. This study also involved three parts. First, there was a four-week, placebo lead-in followed by a 24-week, single-blind treatment period. The third part involved a three-month, double-blind, randomized, withdrawal period. A maximum of 10 mg of terazosin was used. Three patients did not complete the study secondary to adverse events. The final study was an open label dose titration involving 45 patients. They were titrated to 5 mg over a one month period. Assessments were made two months after the beginning of treatment. Five patients withdrew secondary to side effects.

Overall, the four studies involved 163 patients with 10% withdrawing secondary to adverse events. The peak and mean urinary flow rates increased 50% and 46% respectively. Both are statistically significant. There was a statistically significant improvement in obstructive and irritative voiding scores, 67% and 35%, respectively. The changes in blood pressure in patients with a diastolic pressure < 90 mm Hg were not statistically significant, whereas the changes in blood pressure for patients with a diastolic pressure greater than or equal to 90-mm Hg were statistically significant. This suggested that terazosin does not significantly alter blood pressure in normotensive men, where it has a favorable antihypertensive therapeutic response in patients with hypertension. The majority of patients were titrated to a dose equal to or exceeding 10 mg. The three main side effects were dizziness (14%), headache (10%), and asthenia (7%). In addition, baseline clinical and urodynamic parameters were not useful in predicting a clinical response to terazosin.

Lowe and Lepor²⁹ reported 487 patients with symptomatic BPH in a phase III, double-blind, parallel group, placebo-controlled study. This was a two-part study, the first being a four-week, single-blind, placebo lead-in period. The second was a 12-week, double-blind treatment period. Three hundred and fourteen patients entered the second phase of the treatment. Those patients who qualified for the double-blind study were given placebo, 2, 5, or 10 mg of terazosin. The doses of terazosin were titrated over time. Of the 314 randomized patients 264 (84%) completed the

12-week treatment. The indications for withdrawal were similar among all four groups with administrative reasons being the predominant cause.

There were statistically significant decreases in obstructive, irritative, and total symptom scores for all terazosin groups from baseline. The decrease in obstructive scores for the 5 mg and 10 mg terazosin groups were also significantly greater than placebo. The improvement in symptom scores were dose related. The relationship between symptom score and time suggested that the effect of α -blockade occurred within two weeks.

Statistically significant improvement from baseline in the peak and mean urinary flow rates was found for all treatment groups including placebo. However, the 10-mg treatment group had a significantly larger increase from baseline in peak and mean urinary flow rates than the placebo group. There were higher frequencies of certain adverse events seen in the terazosin group but these were not significantly different from placebo. Most common were dizziness (11.4%), asthenia (10.1%), and flu syndrome (6.3%). Blood pressure and pulse were essentially unchanged. However, the 5 mg and 10 mg terazosin groups had significantly larger decreases in diastolic blood pressure but were deemed clinically insignificant. Finally, the improvements in symptom scores did not plateau suggesting that further efficacy may be achieved by dosages exceeding 10 mg. Thus terazosin has been studied in larger groups for a longer period of time than either of the other two major α -blockers previously studied. Overall, efficacy has been documented with only mild adverse side effects. Most importantly it can be given to normotensive males without significant changes in blood pressures or adverse events. Compliance with this once-a-day medication has not been a factor.

CONCLUSIONS

Alternative therapies for the management of BPH have been and will continue to be investigated. α -blockade has been demonstrated in numerous pilot studies to be efficacious in the management of the symptoms related to prostatic obstruction. Studies are currently being undertaken to assess long-term efficacy of terazosin over several years instead of simply several weeks. The optimal candidates and dosage schedules for α -blockade are still being determined. The role of α -blockers in men with hypertension and cardiovascular disease as well as BPH will hopefully be elucidated. This is certainly a promising area for further research. However, TURP is still the gold standard against which alternative therapies must be compared for overall quality of life issues.

REFERENCES

1. Berry SJ, Coffey DS, Walsh PC, et al: The development of human benign prostatic hyperplasia with age. *J Urol* 1984; 132:474-479.
2. Franks LM: Benign nodular hyperplasia of the prostate: a review. *Ann R Coll Surg* 1954; 14:92-106.
3. Roos NP, Wennberg JE, Malenka DJ, et al: Mortality and reoperation after open and transurethral resection of the prostate for benign prostatic hyperplasia. *N Eng J Med* 1989; 320:1120-1123.
4. McNeal JE: Normal histology of the prostate. *Am J Surg Pathol* 1988; 12:619-633.
5. Coffey DS, Walsh PC: Clinical and experimental studies of benign prostatic hyperplasia. *Urol Clin North Am* 1990; 17:461-475.
6. Lepor H, Gup DI, Bauman M, et al: Laboratory assessment of terazosin and α -1 blockade in prostatic hyperplasia. *Urol* 1988; 6:21-26.
7. Caine M: α -adrenergic blockers for the treatment of benign prostatic hyperplasia. *Urol Clin North Am* 1990; 17:641-649.
8. Lepor H: Role of α -adrenergic blockers in the treatment of benign prostatic hyperplasia. *The Prostate Supplement* 1990; 3:75-84.
9. Boreham PF, Braithwaite P, Milewski P, et al: α -adrenergic blockers in prostatism. *Br J Surg* 1977; 64:756-757.

10. Caine M, Perlberg S, Meretyk S: A placebo-controlled double-blind study of the effect of phenoxybenzamine in benign prostatic obstruction. *Brit J Urol* 1978; 50:551-554.
11. Gerstenberg T, Blaabjerg J, Nielsen ML, et al: Phenoxybenzamine reduces bladder outlet obstruction in benign prostatic hyperplasia. *Invest Urol* 1980; 18:29-31.
12. Caine M, Perlberg S, Shapiro A: Phenoxybenzamine for benign prostatic obstruction. *Urol* 1981; 17:542-546.
13. Abrams PH, Shah PJR, Stone R, et al: Bladder outflow obstruction treated with phenoxybenzamine. *Brit J Urol* 1982; 54:527-530.
14. Brooks ME, Sidi AA, Hanani Y, et al: Ineffectiveness of phenoxybenzamine in treatment of benign prostatic hypertrophy. *Urol* 1983; 2:474-478.
15. Griffiths DJ, Shroder FH: Phenoxybenzamine in prostatic obstruction. *Urol Int* 1984; 39:241-242.
16. Ferrie BG, Paterson PJ: Phenoxybenzamine in prostatic hypertrophy. *Brit J Urol* 1987; 59:63-65.
17. Hedlund H, Anderson KE, Ek A: Effects of prazosin in patients with benign prostatic obstruction. *J Urol* 1983; 130:275-278.
18. Martorana G, Gibert C, Damonte P, et al: The effect of prazosin in benign prostatic hypertrophy, a placebo controlled double blind-study. *IRCS Med Sci* 1984; 12:11-12.
19. Kirby RS, Coppinger SWC, Corcoran MO, et al: Prazosin in the treatment of prostatic obstruction. *Brit J Urol* 1987; 60:136-142.
20. Nakamura K, Kawashita E, Osumi Y, et al: Effects of prazosin HCL on the urethral pressure profile in patients with benign prostatic hyperplasia. *Urol Int* 1990; 45 (suppl 1):30-35.
21. Yamaguchi O, Shiraiwa Y, Kobayashi M, et al: Clinical evaluation of effects of prazosin in patients with benign prostatic obstruction. *Urol Int* 1990; 45 (suppl 1):47-55.
22. Chapple CR, Christmas TJ, Milroy EJJ: A twelve-week placebo-controlled study of prazosin in the treatment of prostatic obstruction. *Urol Int* 1990; 45 (suppl 1):18-25.
23. Aoki H, Ohninata M, Tsozaki T, et al: Clinical studies of the effectiveness of prazosin HCL in the treatment of dysuria accompanying BPH. *Urol Int* 1990; 45 (suppl 1): 18.
24. Dunzendorfer U: Clinical experience: symptomatic management of BPH with terazosin. *Urol* 1988; 22:27-31.
25. Lepor H, Knapp-Moloney G, Wozniak-Petrofsky J: The safety and efficacy of terazosin for the treatment of benign prostatic hyperplasia. *Int J Clin Pharmacol Ther Toxicol* 1989; 27:392-397.
26. Fabricus PG, Weizert P, Dunzendorfer U, et al: Efficacy of once-a-day terazosin in benign prostatic hyperplasia: randomized, double-blind placebo-controlled clinical trial. *The Prostate* (suppl) 1990; 3:85-93.
27. Lepor H, Knapp-Maloney G, Sunshine H: A dose titration study evaluating terazosin, a selective once-a-day α 1 blocker for the treatment of symptomatic benign prostatic hyperplasia. *J Urol* 1990; 144:1393-1398.
28. Lepor H, Henry D, Laddu AR: The efficacy and safety of terazosin for the treatment of symptomatic BPH. *The Prostate* 1991; 18:345-355.
29. Lowe F, Lepor H: α -blockade in the management of benign prostatic hyperplasia, in Romas NA, Vaughan ED (eds): *Alternate Methods for the Management for BPH*, Springer Verlag: in press, 1993.

Fetal tissue research and transplantation

FRED ROSNER, MD; HERMAN M. RISEMBERG, MD; PIETER R. KARK, MD; PETER P. SORDILLO, MD, PhD;
ALLEN J. BENNETT, MD; ANTHONY BUSCAGLIA, MD; ERIC J. CASSELL, MD; PETER B. FARNSWORTH, MD;
ABRAHAM L. HALPERN, MD; JOHN B. HENRY, MD; ALLISON B. LANDOLT, MD; LAURENCE LOEB, MD;
PETER ROGATZ, MD; PATRICIA J. NUMANN, MD; FERNANDO V. ONA, MD;
ROBERT E. LOWENSTEIN, MD, PhD; PHILIP H. SECHZER, MD; JONATHAN R. WOLPAW, MD

Fetal tissue research is research using tissue from dead fetuses obtained from spontaneous or induced abortions.¹ Fetal tissue research is different from fetal research. Fetal research is the term generally used to describe research performed on a living, intact fetus inside the uterus. The benefits of fetal research include the development of vaccines, advances in prenatal diagnosis, detection of fetal malformations, assessment of safe and effective medications and the development of in utero surgical therapies.² Fetal tissue research benefits vaccine development, helps evaluate risk factors and toxicity levels of drugs, allows development of cell lines, and provides a source of fetal cells for transplantation as an alternative to whole organ transplantation.

Fetal tissue transplantation has been attempted for a number of disorders including Parkinson's disease, Alzheimer's disease, Huntington's chorea, diabetes mellitus; immunodeficiency disorders such as DiGeorge syndrome, aplastic anemia and leukemia; and severe metabolic disorders such as Hurler's syndrome. Fetal cells are unlike any other tissue in that they engraft easily without producing graft-versus-host disease.³ Fetal cells are able to grow, proliferate and differentiate, and they produce growth factors.³

Further research is needed to determine the potential value of fetal tissue transplantation. Specific ethical guidelines are necessary to ensure that fetal tissue derived from elective abortions is used in a morally acceptable manner.⁴ This essay deals with the history of the governmental ban on fetal tissue transplantation research and the ethical issues involved in such research. This essay does not discuss research on live fetuses,⁵⁻⁶ fetal therapy and surgery⁷ or human embryo research for overcoming infertility.⁸

LEGISLATIVE AND REGULATORY HISTORY OF FETAL RESEARCH AND FETAL TISSUE RESEARCH

Between 1969 and 1973, all 50 states adopted the Uniform Anatomical Gift Act (UAGA), which authorizes the gift of all or part of a human body after death for specified purposes. The Act allows tissue from dead fetuses to be used for research or for therapeutic purposes.

Prepared as an educational and informational report by the Committee on Bioethical Issues of the Medical Society of the State of New York, Lake Success, NY.

Address correspondence to Dr Rosner, Director, Department of Medicine, Queens Hospital Center Affiliation of the Long Island Jewish Medical Center, 82-68 164th Street, Jamaica, New York 11432.

"Research using fetal tissue follows the scientific tradition of medical inquiry and of the study of human pathology as in the long-standing practice of autopsy."¹ However, in response to the 1973 *Roe v Wade* decision of the Supreme Court legalizing abortion, many states proposed legislation to ban fetal research.

In 1974, the National Research Act established the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission's report to Congress in 1975 with recommendations on the establishment of regulations on fetal research resulted in regulations being issued by the Department of Health, Education, and Welfare (now called the Department of Health and Human Services) governing fetal research. In 1985, the reauthorization bill for the National Institutes of Health (NIH) placed a three-year moratorium on fetal research above the "minimal risk" standard and established the Congressional Bioethics Board to study the nature, advisability, biomedical, and ethical implications of exercising the waiver provision of the fetal research regulations.

In 1985, a Swedish team of surgeons successfully transplanted autologous fetal adrenal tissue into patients with Parkinson's disease.⁹ Two years later, Mexican surgeons reported further success with a modified version of the Swedish technique.¹⁰ In October 1987, the NIH submitted a request to Assistant Secretary for Health, Robert Windom, for approval of a clinical experiment at NIH that would involve the transplantation of human fetal neural tissue derived from an induced abortion into the brain of a patient suffering with Parkinson's disease. In March 1988, Dr Windom denied the request and placed a moratorium on all federal funding of transplantation research with fetal tissue derived from induced abortions. Dr Windom also asked the NIH to convene a special ad hoc advisory panel to examine comprehensively the medical, legal, and ethical propriety of fetal tissue research. He posed questions to the panel about the morality of induced abortions for fetal tissue: whether the research would encourage abortion; whether and how consent could be obtained; what kinds of prohibitions should be placed on donations and procurement of the tissue; and whether the research in fact had reached a stage to warrant transplantation.

A Human Fetal Tissue Transplantation Research Panel was convened, consisting of 21 people with a wide range of experience in scientific, legal and ethical matters and with varying views on the morality of abortion. The Panel

submitted a report in December 1988 to the Advisory Committee of the Director of the NIH. The Advisory Committee concluded on current evidence that fetal tissue research could indeed lead to medical treatment that would enormously help many millions of people and that the use of fetal tissue from induced abortions was acceptable public policy with proper safeguards. The Advisory Committee said that it was possible and appropriate to separate the issue of the morality of elective abortions from the issue of allowing fetal tissue to be used in research on therapeutic transplantation. The Advisory Committee unanimously recommended that the moratorium be lifted. Nevertheless, on November 2, 1989, Department of Health and Human Services (DHHS) Secretary, Louis Sullivan, overrode the NIH advisory panel and extended the moratorium indefinitely.

The issue of research on human fetal tissue became completely politicized.¹¹ In the view of proponents of research, "politics had taken precedence over sound policy and life-saving research."¹²

Debate about fetal tissue transplants continued despite the government's decision not to support it. An underlying concern was that women might choose to become pregnant and intentionally abort their fetuses to have them used for fetal tissue transplantation. At a congressional hearing early in 1990 called to oppose the Bush administration's decision not to fund fetal tissue transplantation projects, proponents of the research argued that the use of fetal tissue can be separated from the decision to abort. Opponents, however, argued that the two were inextricably linked. California representative Henry A. Waxman, a strong supporter of both abortion rights and fetal tissue transplantation, said the DHHS was denying millions of people with debilitating diseases the potential research benefits by refusing to fund such transplants.¹³

Additional reports appeared in the medical literature about the alleviation of symptoms of Parkinson's disease with fetal neural implants.¹⁴⁻¹⁵ Many in the scientific community, including the AMA, argued that the ban stifles research that could lead to advances in the treatment of a variety of diseases such as Alzheimer's disease and dozens of genetic disorders. In poignant testimony, a husband and wife who oppose abortion told a Congressional subcommittee on April 15, 1991, how they nevertheless agreed to use tissue from an aborted fetus in a desperate attempt to save their unborn son from Hurler's syndrome, a fatal genetic disease.¹⁶ The Institute of Medicine issued a report which points out that the government's moratorium on fetal research hampers progress in medically assisted conception.¹⁷ The same ban also hampers research which might benefit patients suffering from acquired immunodeficiency syndrome.¹⁸

The recently Bush appointed NIH director expressed views in favor of United States funding of research using fetal tissue, and cited a lack of federal leadership. The American College of Obstetricians and Gynecologists and the American Fertility Society announced plans early in 1991 to establish a national ethics advisory board to offer guidelines for research and protocols involving human embryos and fetal tissue. A coalition of groups that want to find treatments for Parkinson's disease prepared to file suit against DHHS Secretary, Louis Sullivan, because of his ban on federal funding of research that uses fetal tissue.¹⁹

In July 1991, the House of Representatives passed a bill (HR2507) to restore federal funding for human fetal tissue

research. In the proponent's view, this represented a significant advance in attempts to overturn the federal fetal tissue ban, although the bill still contained two important restrictions. It required women who are willing to donate fetal tissue to certify that they did not have an abortion with the intent to donate. The bill also required researchers to keep the certifications on file and available for government audit.²⁰

In April 1992, the US Senate voted overwhelmingly to lift the moratorium on federally funded fetal tissue transplantation research. The Senate bill (S1523) differed in important ways from the bill passed by the House. For example, S.1523 placed the burden on the health professional, as opposed to the patient, to certify that consent for the abortion was obtained before discussion of the donation of fetal tissue. It required that a woman be informed of the health provider's interest in the research to be conducted with the donated tissue and of any known risks to her privacy or medical interests. In addition, finally, two important provisions were deleted: the requirement that a woman who consents to donate certify that her reasons for aborting do not include the desire to donate fetal tissue, and the requirement that the woman's signed consent forms be forwarded to the researcher(s) and made available for audit by government officials.

In response to the Bush administration's concern that fetal tissue transplantation research will encourage women to undergo abortions for the purpose of donating fetal tissue, both H. R. 2507 and S.1523:

- Prohibit women from being paid for any tissue they donate;
- Prohibit women from designating the recipient of the fetal tissue;
- Require that the attending physician obtain consent for the abortion prior to requesting or obtaining consent for the donation of fetal tissue.²¹

As expected, President Bush vetoed the legislation after the House and Senate ironed out differences in the two bills. The 87 to 10 Senate and 274 to 144 House vote suggested that they might be able to override the presidential veto. In an attempt to prevent this, President Bush directed Health and Human Services Secretary Louis Sullivan to create a national fetal tissue bank to assist researchers in the field. The tissue, however, was to come only from ectopic pregnancies and spontaneous abortions, not induced ones.²² The revised NIH bill would allow sufficient time for the tissue bank to demonstrate whether it can meet the needs of the research community. If the bank fails to be a viable source, researchers would be free to seek tissue from alternative sources. Opponents of this approach argue that tissue from such sources as spontaneous abortions and ectopic pregnancies is both difficult to obtain and rarely suitable for transplantation. Science and politics collided on this issue.²³

On June 24, 1992, the House failed to override the Presidential veto on fetal tissue research. The ban on federally financed research on the use of tissue from aborted fetuses remained in effect. A handful of researchers in the United States pursued such research with private funds.²⁴ The ban was finally lifted soon after Clinton was elected.

PHILOSOPHICAL ISSUES IN FETAL TISSUE RESEARCH

It is important to emphasize that the philosophical issues for or against the legalization of abortion are different issues than those involving fetal tissue research. Many prominent opponents of legalized abortion are supporters

of fetal tissue research. Even many of those who believe abortion is immoral and concede that fetal tissue research might have the indirect effect of increasing the frequency of abortion, argue that scientists have the right to pursue research without the interference of society or government as long as the scientists are not themselves impinging directly on the rights of others. The fundamental tenet of our political system is the inalienable right of individuals to lead their lives and pursue their goals independent of the desires of the society at large. These rights extend to scientific researchers, as well. Both liberals and conservatives might question why the state presumes to interfere with activities of physicians and scientists who are not endangering any other individuals and whose research might save countless lives.

ETHICAL ISSUES IN FETAL TISSUE TRANSPLANTATION

In the early 1970s, the question of doing research with fetal tissue was overshadowed by the international debate about the morality of abortion. In the 1990s, the question of fetal tissue transplantation still remains associated with that of induced abortion even though fetal tissue research should be viewed primarily within the more general context of transplanting organs and tissues.²⁵ Current law allows the use of nonviable, spontaneously aborted fetuses for therapeutic transplantation. However, such a source is neither large nor reliable. Induced abortions would provide a more reliable and larger supply of potential fetal transplant material. However, the question of the morality of induced abortion continues to hamper meaningful political and social policy decisions on this issue.

The main moral question is: Should doctors be allowed to use tissue from intentionally aborted fetuses to alleviate or possibly cure an otherwise hopeless or incurable disorder? There seems to be little objection to the use of tissue of spontaneously aborted or miscarried fetuses. There is strong objection, however, to a woman becoming pregnant for the sole purpose of providing fetal tissue to treat herself or a family member.²⁶ Other ethical concerns include the possibility that a woman may be influenced to have an abortion to sell the fetal tissue for financial gain. Other women might decide to terminate their pregnancy because of an altruistic desire to help a stranger in need of a fetal tissue transplant.

The architecture of the fetal tissue transplant controversy, in one writer's opinion, is similar to that of many bioethical debates, with a novel twist because of the contested status of the fetus and abortion.²⁷ Respect for the need of sick patients therefore appears to conflict with respect for prenatal human life and larger societal concerns. In addition to the question of abortion itself, there are moral and social issues about the retrieval of tissue from dead *v* live fetuses; about how to procure tissue, including questions of consent, and of commerce in obtaining and distributing fetal tissue. Most ethicists view the use of tissue from the dead fetus for therapy to be morally acceptable. In such a case, salvaging of fetal tissue is no different than the salvaging of an organ from any other cadaver.²⁸ There is a potential commercial gain for those involved in the retrieval, storage, testing, preparation, and delivery of fetal tissues. It would greatly reduce the possibility of improper influence on a woman to acquire her consent for donation of aborted fetal remains if such tissue were only available through non-profit institutions.⁴

The 1988 NIH Advisory Panel described above debated the moral relevance of using tissue from induced abortions.²⁹ The opinion of the majority acknowledged the moral problem of abortion but also acknowledged that abortion is legal and the strong therapeutic implications of fetal tissue transplantation. The majority approved of fetal tissue research if the woman gives consent and if the use of the tissue is completely dissociated from the decision to terminate the pregnancy:

The opinions of the minority took issue on every one of these points. They considered abortion morally wrong, regardless of its legal status or the therapeutic utility of the tissues provided. They argued that authentic informed consent was not possible since a woman who decided to terminate a pregnancy could not be considered to be acting in the fetus' interests. They denied the practicality of isolating the decision to terminate a pregnancy from the decision to donate tissue. They saw helping another person as a powerful inducement to abortion. They predicted *de facto* complicity with the abortion industry in the procurement of fetal tissues and in the profits that would accrue.³⁰

Debate continues in the medical and ethical literature. One writer suggests that fetal tissue transplantation will be circumscribed by medical and moral limits and that it will not erode important ethical values. He points out that the pace of scientific research must not preempt public debate or a verdict consistent with societal values.³¹ In contrast, another author claims that transplantation of tissue from fetal cadavers threatens ethical values and social ethics in complex and subtle ways. Work with fetal tissue requires restraints that can prevent normative and attitudinal shifts yet permit pursuit of medical benefits for those in desperate need.³² Other authors contend that whether or not abortion is morally justified, use of human fetal tissue is justified in certain circumstances. The rationale, both for transplantation of fetal tissue and for limitation is based on the ethical principles of respect for autonomy and a balance of harm and benefit that gives priority to those most affected.³³ These authors suggest that moral requirements for fetal tissue transplantations include consent of a proxy, a significant research or therapeutic goal, and evidence that other means of obtaining the goals are not available.

The Committee on Ethics at Stanford University Medical Center believes that the use of human fetal tissue is not itself objectionable.³⁴ However, the use of fetal tissue should not be allowed to encourage pregnancies and abortions that would not occur otherwise. Patients and physicians should not gain financial benefit from the aborted fetuses. The committee also concluded that human fetal tissue should be treated with the same respect given to full cadavers, and its use should be governed by the same legal rules. In addition, the committee felt that the use of fetal tissue from spontaneous miscarriages and from abortions induced because of risk to the mother's life is ethically unobjectionable.

The Council on Scientific Affairs and the Council on Ethical and Judicial Affairs of the American Medical Association made recommendations about the medical applications of fetal tissue transplantation so that fetal tissue derived from elective abortions would be used in a morally acceptable manner.⁴ The recommendations state that the use of fetal tissues for transplantation purposes is ethically permissible when the following apply:

1. The Council's guidelines on clinical investigation and organ transplantation are followed;

2. Fetal tissue is not provided in exchange for financial remuneration;
3. The recipient of the tissue is not designated by the donor;
4. The decision to abort is made before discussion of fetal tissue transplantation is initiated;
5. Decisions about techniques and timing of abortion are based on concerns for the woman's safety;
6. Health care personnel involved in the abortion do not participate in or benefit from the fetal tissue transplant;
7. Informed consent on behalf of both the donor and the recipient is obtained in accordance with applicable law.

These guidelines, if followed, separate the decision to have an abortion from the decision to donate the dead fetal tissue and provide "safeguards to reduce any motivation, reason, or incentive by the woman to have an abortion."⁴

REFERENCES

1. Lehrman D: *Summary: Fetal Research and Fetal Tissue Research*. Washington DC, Assn. Amer Med Coll, 1988.
2. Hansen JT, Sladek JR, Jr: Fetal research. *Science* 1989; 246:775-779.
3. Consultants to the Advisory Committee to the Director: *Report of the Human Fetal Tissue Transplantation Research Panel*. Bethesda, MD, National Institutes of Health, 1988.
4. Council on Scientific Affairs and Council on Ethical and Judicial Affairs: Medical applications of fetal tissue transplantation. *JAMA* 1990; 263:565-570.
5. Fletcher JC, Schulman JD: Fetal research: the state of the question. *Hastings Center Rep* 1985 (April); 15:6-12.
6. Tiefel HO: The cost of fetal research: ethical considerations. *N Engl J Med* 1976; 294:85-90.
7. Rosner F, Bennett AJ, Cassell EJ, et al: Fetal therapy and surgery: fetal rights versus maternal obligations. *NY State J Med* 1989; 89:80-84.
8. Editorial: Embryo research. *Lancet* 1985; 1:255-256.
9. Backlund EO, Granberg PO, Hamberger B, et al: Transplantation of adrenal medullary tissue to striatum in Parkinsonism: first clinical trials. *J Neurosurg* 1985; 62:169-173.
10. Madrazo I, Drucker-Colin R, Diaz V, et al: Open microsurgical autograft of adrenal medulla to the right caudate nucleus in two patients with intractable Parkinson's disease. *N Engl J Med* 1987; 316:831-834.
11. Annas GJ, Elias S: The politics of transplantation of human fetal tissue. *N Engl J Med* 1989; 320:1079-1082.
12. Adams B: Restoring hope: lifting the ban on fetal tissue transplantation research. *Acad Med* 1992; 67:246-247.
13. Gianelli DM: Fetal tissue transplant debate continues. *Amer Med News* April 13, 1990, pp1,27.
14. Lindvall O, Brundin P, Widner H, et al: Grafts of fetal dopamine neurons survive and improve motor function in Parkinson's disease. *Science* 1990; 247:574-577.
15. Freed CR, Breeze RE, Rosenberg NL, et al: Transplantation of human fetal dopamine cells for Parkinson's disease: results at 1 year. *Arch Neurol* 1990; 47:505-512.
16. Hilt PJ: Fetal tissue used: anguish behind a medical first. *NY Times*, April 16, 1991, ppA1,C6.
17. Gianelli DM: US Rule on fetal research hampering IVF report. *Amer Med News*, Dec 1, 1989, pp1,35.
18. Kolata G: US rule on fetal studies hampers research on AZT. *NY Times*, August 25, 1991; pL20.
19. Powlledge TM: Springtime for fetal tissue research? *Hastings Center Rep* 1991 (March-April); 21: 5-6.
20. Kearney W, Vawter DE, Gervais KG: Fetal tissue research and the misread compromise. *Hastings Center Rep* 1991 (Sept-Oct); 21:7-12.
21. Vawter DE: Fetal tissue update. *Hastings Center Rep* 1992 (March-April); 22:3.
22. Leary WE: Bush to set up research banks for fetal tissue. *NY Times*, May 20, 1992, ppA1,16.
23. Greenberg DS: When science and politics collide. *Lancet* 1992; 339: 1469-1470.
24. Perrone J: Researchers circumvent fetal tissue transplant funding ban. *Amer Med News*, June 8, 1992, pp3,32.
25. Walters L: Ethical issues in fetal research: a look back and a look forward. *Clin Res* 1988; 36:209-214.
26. Gianelli D: Bearing a donor? Ethical concerns raised over having a baby for marrow match. *Amer Med News*, March 2, 1990, pp3,9.
27. Robertson JA: Rights, symbolism and public policy in fetal tissue transplants. *Hastings Center Rep* 1988 (Dec); 18:5-12.
28. Jonsen AR: Transplantation of fetal tissue: an ethicist's viewpoint. *Clin Res* 1988; 36:215-219.
29. Report of the Human Fetal Tissue Transplantation Research Panel: Washington DC, US Govt Printing office, 1988.
30. Pellegrino ED: Ethics. *JAMA* 1989; 261:2843-2845.
31. Fine A: The ethics of fetal tissue transplants. *Hastings Center Rep* 1988 (June/July); 18:5-8.
32. Nolan K: Genug ist genug: a fetus is not a kidney. *Hastings Center Rep* 1988 (Dec); 18:13-19.
33. Mahowald MB, Silver J, Ratcheson RA: The ethical options in transplanting fetal tissue. *Hastings Center Rep* 1988 (Feb); 17:9-15.
34. Greely HT, Hamm T, Johnson R, et al: The ethical use of human fetal tissues in medicine. *N Engl J Med* 1989; 320:1093-1096.

Joseph Peter Hoguet, MD

A courageous New York surgeon

PASCAL JAMES IMPERATO, MD

Joseph Peter Hoguet, MD, achieved renown in the first half of the 20th century not only for his superb clinical skills as a surgeon, but also for his remarkable courage under adversity. During the 1920s, when he was at the apex of his medical career, he was considered one of the finest surgeons in the country. As one of New York City's leading surgeons, he treated numerous physicians and their families and was regularly called on to assume the care of patients who other surgeons considered hopeless. When his career as a surgeon was suddenly and unexpectedly brought to an end it was a tragedy not only for him personally, but also for his patients, family, and colleagues.¹

EARLY YEARS

Hoguet was born on August 16, 1882, in Long Branch, NJ, into a French Catholic family that had first settled in the United States in the early 19th century.² The son of Robert J. Hoguet and Marie Noel, he was the third of six children (Ramsay, Robert, Joseph Peter, Rene, Marguerite, and Marie). His two older brothers became lawyers and Robert later served as chairman of the board of directors of the Emigrant Industrial Savings Bank.³ Named Joseph Pierre at birth, Hoguet later interchangeably used this name with those of Joseph Peter and J. Peter.

Hoguet's great-great grandfather, Robert J. Hoguet, emigrated from France to Dublin, Ireland, where he became a leading merchant. He later settled in New York City where his son, Anthony, set up the mercantile firm of Hoguet and Son on Maiden Lane. Anthony's son, Henry L., who was Hoguet's grandfather, became the president of the Emigrant Savings Bank and a partner in Wilmerding, Hoguet and Co., He was also a trustee of Old Saint Patrick's Cathedral.³

The Hoguets became a socially prominent family in New York City whose wealth was based on banking and business. Hoguet was raised in comfortable circumstances and was educated at Sachs Collegiate Institute on 59th St in Manhattan. Given that his family role models were bankers, businessmen, and lawyers, it seemed almost a certainty that he would choose one of these careers.²

COLLEGE AND MEDICAL SCHOOL EDUCATION

Hoguet entered Harvard in 1900, the year after his older brother Robert graduated.^{4,5} He later described, with a tinge of humor, his years at Harvard and those which followed in medical school.⁴

I left college in the spring of 1903 as I had somehow or other managed to get together the requisite number of points for my AB which I took with the class in the spring of 1904. In the fall of 1903, I started in the weary grind of learning medicine in the College of Physicians and Surgeons in New York City. After four years of real work, Columbia presented me with the degree of MD, which I have managed to keep ever since.

EARLY MEDICAL TRAINING

On graduating from Columbia University College of Physicians and Surgeons (P & S) in 1907, Hoguet did three years of internship in surgery at St Luke's Hospital in New York City. There he distinguished himself as both an astute clinician and as a superb technician admired for his speed in completing surgical procedures. He characterized his three years at St Luke's as "very enjoyable."

TSAR NICHOLAS II STARTS HOGUET ON A HOBBY

After completing his residency in surgery at St Luke's, Hoguet was invited to sail on the yacht of Mrs Ogden Goelet. Mrs Goelet was then a matriarch of New York and Newport society and planned to sail in the Black Sea for health reasons. While this trip afforded Hoguet a much needed vacation, it also provided Mrs Goelet, whose health was precarious, with a personal physician in case of emergencies. While in the Black Sea, Mrs Goelet invited Tsar Nicholas II on board and presented Hoguet to him. The Tsar was much taken with Hoguet and as a parting gift gave him two magnificent Russian wolfhounds which he had taken on board. Hoguet brought the dogs back to New York and eventually established a show kennel of some 40 hounds at his home in Locust Valley on Long Island.⁶

PRIVATE PRACTICE AND WORLD WAR I

In 1910, Hoguet established an office at 40 East 41st St and joined the staff of the Hospital for the Ruptured and Crippled (later the Hospital for Special Surgery) and that of the French Hospital. He eventually rose to the rank of Surgeon at the French Hospital in 1925 and to the same rank at the Hospital for the Ruptured and Crippled in 1926. However, his early years in practice were not easy. He later said:⁴

... the start of practice ... was not so good. However, I went at it pretty hard and when there was no private practice I got all the hospital jobs I could lay my hands on, and learned the surgical business by working night and day in the hospitals. Little by little I began to hoodwink more and more people into thinking that I knew something, and, in 1912, jumped into matrimony, and then had to work harder yet.

Address correspondence to Dr Imperato, Editor, *New York State Journal of Medicine*, 420 Lakeville Rd, Lake Success, NY 11042.

Although he later became a consultant at several other hospitals including Bellevue, Mary McClelland in Cambridge, New York, Misericordia, Memorial, and North Country Community in Glen Cove, New York (later the Community Hospital at Glen Cove), he largely confined his clinical activities to the French Hospital and to the Hospital for the Ruptured and Crippled. In 1917, he was named Chief Surgeon at the French Hospital, a position he held for many years until 1930.^{2,7}

After the outbreak of World War I in 1914, Hoguet volunteered his services at the American Ambulance Hospital in Neuilly-sur-Seine, France in the Spring of 1915, where he worked for a few months under James A. Blake, MD (1865–1937), who had been professor of surgery at P & S from 1903 to 1913. Blake, who was a distinguished surgeon, had been Hoguet's professor of surgery at P & S and his teacher during his surgical residency at St Luke's. Blake held the rank of attending surgeon at St Luke's and considered Hoguet one of his protégés. Blake was an 1889 graduate of P & S who was also trained in anatomy, a subject which he taught to P & S medical students from 1891 to 1900.^{8,9}

On his return to the United States, Hoguet joined the US Army Medical Corps as a captain. They were pleased to have someone with surgical experience in the then current war and he was delighted to have a steady job. He modestly summarized his years in the Army by saying, "I spent most of the time at the Rockefeller Institute teaching war surgery to the new arrivals in the army."⁴ However, his achievements at the Rockefeller Institute were significant. He participated in research which led to the development of the Carrel-Dakin Solution. He was also assigned to the War Demonstration Hospital Number 1 in New York City where he taught the Carrel-Dakin method of wound disinfection. He remained at the War Demonstration Hospital until he was discharged from the Army on December 26, 1918. He then re-entered private practice.

AN EXPERT ON HERNIA REPAIR

Hoguet's association with academic surgeons of Blake's caliber and researchers at the Rockefeller Institute nurtured an interest in clinical research. His principal mentor, once he left the US army and re-entered private practice, was William B. Coley, MD (1862–1928). Coley, like Blake, was a leading surgeon in New York City. An 1888 graduate of Harvard Medical School, he taught surgery for several years at P & S and in 1910 became professor of clinical surgery at Cornell University Medical College. At the same time, he became the attending surgeon of the Hernia Department at the Hospital for the Ruptured and Crippled. Although Coley had gained a reputation as an expert in the treatment of malignancies, he was also a pioneer in the field of hernia repair. At the time, many physicians advocated mechanical treatments for inguinal hernia in children. Coley, however, showed through prospective studies that such treatments were not successful, thus refuting the claims of the advocates of non-surgical intervention.^{10,11}

Coley was Hoguet's senior by 20 years. He had known Hoguet at P & S, knew of his exceptional surgical skills from Blake and others, and quickly made him his protégé. Working under Coley, Hoguet rapidly acquired an enormous clinical experience in hernia repair. However, during their early association, Hoguet also shared Coley's interest in the treatment of malignancies, especially sarcomas. The

two of them, for example, co-authored a major paper in 1916 entitled *Melanotic Cancer*.¹² While Coley continued his interest in cancer treatment research, especially through the use of bacterial toxins, Hoguet experimented with modifications of the Bassini procedure, which by that time had become the standard operation for inguinal hernia. In 1918, he and Coley reported on the techniques and results of 8,589 herniorrhaphies performed at the Hospital for the Ruptured and Crippled between 1891 and 1918.¹³ Two years later, Hoguet reported on the results of surgery in 142 cases of direct hernia, and in 1923 reported on the results of 2,468 repairs of different types of hernia performed by himself between 1910 and 1923.^{14,15}

In 1918, Hoguet became an assistant clinical professor of surgery at Cornell University Medical College. A 1921 graduate of the school later made the following observations about him:¹⁶

He was considered one of the finest and fastest surgeons in the city and an expert on hernia repair. He was a wonderful technician and an inspiring teacher. Other physicians always spoke in superlatives of him and we students were awed that so young a surgeon could be so knowledgeable and skillful.

Hoguet's innovations in hernia repair were not restricted to technical procedures. He also promoted the use of local anesthesia in cases of strangulated inguinal hernia, and in patients in whom general anesthesia was contraindicated because of age or co-morbidities. He also experimented with the use of nitrous oxide and oxygen along with morphine and magnesium sulfate in several hundred cases. He reported that this latter form of anesthesia provided sufficient analgesia to permit careful dissection of the field. It had the advantage over ether in that most patients gained consciousness within a few minutes after the termination of surgery and suffered no side effects.¹⁵

A SURGICAL INNOVATOR

Hoguet was widely respected for his boldness in developing new surgical approaches to difficult problems. Among these was a successful procedure for reconstructing hip-joints damaged by tabetic arthropathy (Charcot's Disease). Although Royal Whitman had reconstructed knee joints affected by Charcot's disease, Hoguet was the first to attempt reconstruction of a hip joint. Reporting in the *Annals of Surgery* in 1926, he described the removal of the head of the femur, the insertion of the smoothed upper end of the shaft of the femur into the acetabulum and the repositioning of the great trochanter and the attached gluteal muscles. The patient made an excellent recovery and was free of pain and ambulatory a few weeks post-operatively. Hoguet followed this patient for a full two years before reporting his results in the medical literature.¹⁷

In 1924, Hoguet promoted the use of human fascia as suture material in hernia surgery. He reserved its use for large direct and indirect inguinal hernias, and umbilical and ventral hernias. This technique had been devised by William E. Gallie, MD, a Toronto surgeon who had spent a year of residency training at the Hospital for the Ruptured and Crippled in 1905. While Hoguet advocated the use of a patient's own thigh fascia, in instances where this was not strong enough, he used fascia from other patients simultaneously undergoing surgery. While we now know that the use of the latter clearly carries the risk of transmission of a number of diseases, especially hepatitis-B, at the time,

Hoguet was only concerned about syphilis. He found human fascia to be a superior suture material to animal fascia as he laced it back and forth over the suture line where it eventually took as a human graft. In 1924, Hoguet and others performed 48 herniorrhaphies using human fascia as sutures. Eventually, Hoguet described a series of 443 patients in whom he had used this technique. Recurrences occurred in only 28 (6.3%).¹⁸

A CONSULTANT TO OTHER PHYSICIANS

Hoguet's knowledge and skills extended to all areas of surgery, especially gastroenterological surgery. His speed and skill were especially admired with regard to cholecystectomies and appendectomies. He was able to complete an appendectomy in 20 minutes and once told an audience that he could match that time even if he had to remove a man's appendix on the sidewalk with the use of a local anesthetic.

While he was formally a consultant to the Mary McClelland Hospital in Cambridge, New York, where his mentor, Coley, was chief surgeon and to other hospitals such as the North Country Community Hospital in Glen Cove, which was near his Long Island home in Locust Valley, he also consulted on cases at numerous hospitals in the New York City area (Fig 1).

The uncle of this writer, who was a 1921 Cornell University Medical College graduate, said the following of him in this regard:¹⁶

I always called on Hoguet for difficult cases and he was always willing to come over to Brooklyn to do the surgery for me. My patients didn't know who Hoguet was and most did not appreciate the fact that he was one of the best surgeons in the city. I used to assist him and always marvelled at his skill. His fingers moved around the operating field with amazing speed and without any hesitation. Once the operations were over, Hoguet would leave and I would see the patients in the recovery room. Many patients wrongly assumed that I had performed the surgery since Hoguet never saw them during the post-operative period. He used to joke that he was my "ghost surgeon" and tease me about getting credit for his excellent results.

Physicians at many hospitals called on Hoguet or else referred their patients to him. Such was their confidence in him that they often referred their own family members to him. For example, this writer's father was referred in 1926 by a physician brother for the repair of bilateral inguinal hernias.¹⁹ In other instances, Hoguet was called in emergencies or when an unusual problem presented itself. His son recalled the following unusual case:⁶

During the 1920s, the Prohibition years, gangland killings were not uncommon in New York. One evening en route to Bellevue Hospital, on which staff my father served, a man was machine gunned a block or so from Bellevue and as a matter of fact a few hundred yards from Dad. He was brought to the hospital, and my father operated on him, removing several bullets from his body. The proximity to Bellevue and prompt surgical attention may well have saved his life.

Some weeks later, this well known underworld figure asked to meet the surgeon who had saved his life. As Dad recounted it, he thereafter admonished friends to show him great respect as the gangster allegedly said to Dad "Listen Doc, you and I make our living a little differently—you save lives and I do the reverse—I generally charge \$500 but if ever you need to get rid of a friend—for you it's for free."



FIGURE 1. Joseph Peter Hoguet, MD, as he appeared in the 1930s (courtesy J. Peter Hoguet).

A SUCCESSFUL CAREER AND PRIVATE LIFE

As the 1920s drew to a close, Hoguet was 47 years old and at the peak of his career. He was chief of surgery at the French Hospital, an attending surgeon at the Hospital For the Ruptured and Crippled and a consultant at several other hospitals. He was a member of many medical societies and a Fellow of the American College of Surgeons.

The demands on his professional skills had by this time proven so great that he had begun to decline consultations and refer them to junior colleagues. There were few surgeons in New York City who could match his professional success. Yet, he was modest about his accomplishments when describing them to his Harvard classmates in 1929. "Back into practice after the armistice, and that's what I have been doing ever since. I am attending surgeon to two of the hospitals in New York and spend considerable time teaching at the Cornell Medical School so that time rarely hangs heavily on my hands."

He also provided a glimpse into his private life during the 1920s:⁴

I am not much of a hand at vacations but I like to take some week ends off, and when I get very tired like to take a trip somewhere.

Three years ago my wife and I toured this country for two months, and last spring we went to Europe for a little while. Every once in a while during the year I go off shooting for a few days, but the profession is a very exacting taskmaster so that I generally have to get back to work in a short time. I hope to continue the same kind of life for about another twenty years, and then I shall be too old to work, and shall either have accumulated enough to retire to the farm or else my boys will have to support me.

Hoguet and his wife, Helen Noel Gourd, who had been married at St Patrick's Cathedral in 1912, had four children, Lawrence, Nancy, Roland, and J. Peter and lived in a comfortable apartment at 133 E 64th St in Manhattan. They were especially proud of their country home in Locust Valley, Long Island, which had been designed and built according to their specifications. There, he kept a show kennel of 40 wolfhounds and enjoyed shooting. He also had an avid interest in New York history and according to one of his sons "...became an avid collector of all types of written material on the subject."⁶

During the 1920s, Hoguet received several honors. However, the one he especially cherished was a gold medal awarded to him by the French government for "service to mankind."

A TRAGIC ACCIDENT

On the evening of December 27, 1930, Hoguet, his wife, and some guests left the Locust Valley house by car on their way to dinner. As Hoguet slowly drove along an icy dirt road adjacent to his house, his car skidded into an embankment and turned on the driver's side. His left arm was crushed by the top of the door before it could be withdrawn. No one else in the car suffered any injuries.²⁰ Hoguet was taken to North Country Community Hospital in Glen Cove. His forearm was so badly crushed that the only recourse was a below the elbow amputation. Amputation effectively meant that Hoguet's career as a surgeon was over. The professional life that he had so carefully built up over two decades was suddenly brought to an end.

The news of this tragedy spread quickly through New York's medical community. There was little that friends and colleagues could do to console him, since his professional options were now so few. He, himself, had a difficult time adjusting to this tragedy, but the courage that had carried him through life thus far enabled him to cope as best he could.

In 1930, Hoguet resigned as chief of surgery at the French Hospital and as an attending surgeon at the Hospital for the Ruptured and Crippled. In commenting on the accident, his friend, William B. Coley, MD, said the following when Hoguet resigned from the staff of the Hospital for the Ruptured and Crippled in the late summer of 1930:²¹

While the hospital would gladly have retained him on staff, it recognized the wisdom of his decision to withdraw entirely from surgery and to devote himself to other pursuits. Dr Hoguet had served on the staff since 1910 and held the position of attending surgeon for five years. During this time, he wrote numerous papers on the subject of hernia in one of which he introduced a new and original method to deal with the hernial sac when operating for direct inguinal hernia. Following his resignation as a member of the staff, Dr Hoguet was elected to the board of managers.

FINDING A NEW PROFESSIONAL CAREER

Hoguet's resignations from the active staffs of hospitals and especially his relinquishing of the leadership of the

Department of Surgery at the French Hospital, provide insights into the structure of medical care at the time. Departmental chiefs were clinically very active, admitted large numbers of patients to the hospital, and had few administrative or managerial duties. Several decades later, however, hospital-based medicine in the United States requires that chiefs of service devote enormous amounts of time to administrative and managerial duties. Yet, there was little choice for Hoguet given that chiefs of surgery then primarily operated.

There were few professional options open to Hoguet. The broad range of alternative careers in administrative medicine, which are so much a part of the scene in the late 20th century, did not exist then. In addition, the Depression which followed the Wall Street crash of 1929, greatly reduced demands for physician services. As the 1930s progressed, even once busy surgeons began functioning as general practitioners and treating colds and sore throats for 25¢ a visit just to survive.

There was little prospect for Hoguet making a living as a general practitioner. Friends and colleagues agreed to help as best they could. As one observed:¹⁶

He lost his arm and never operated again. However, I and others used to call on him as a consultant in later years and ask him to examine patients and offer advice. This did not provide him with much of an income, but it showed him that we cared and that we still respected and admired him as a surgeon.

Hoguet's financial burdens were enormous. His loss of professional income was aggravated by his loss of accumulated capital in stocks because of the Depression. Eventually, he had to sell the Locust Valley house, which he and his wife Helen loved so much, to satisfy the mortgage. At the time of his accident his children ranged in age from 9 to 16 years. The need to support them and provide them with a good education was always uppermost in his mind.²⁰

In 1935, some well-meaning friends made him a partner in a Wall Street brokerage house. However, there was little business in equities then and as his son observed: "... my father's heart just wasn't in business—he was too much of a professional medical man."²⁰

Hoguet adjusted as best he could to his disability, although he never spoke of the accident to his family in subsequent years. He learned to tie a bow tie and designed a brace for his stump which allowed him to shoot a shotgun.

MEDICAL DIRECTOR OF THE NEW YORK WORLD'S FAIR

In the mid-1930s, Grover Whalen, who was then the New York administrator for the National Recovery Administration, proposed that New York City sponsor a World's Fair to revive its economy. Whalen, who was a businessman, promoter, and New York City's official greeter, was at the time chairman of the board of the Schenley Products Corporation. Previous to this he had been the Police Commissioner of New York City under Mayor James Walker. Whalen sold the idea of a world's fair to New York City's political and business leaders. He was elected president of the nonprofit corporation to organize the fair and promoted it as "The World of Tomorrow" and as the sesquicentennial of the inauguration of President George Washington on April 30, 1789, in New York City.²²

In 1937, before the New York World's Fair opened, Hoguet was appointed medical director and administrative assistant. Through his attorney, Louis G. Imperato, he negotiated a contract with Whalen to provide medical



FIGURE 2. Joseph Peter Hoguet, MD (left), presenting Mary B. Allison, MD, (right) with medical supplies at the headquarters of the Medical and Surgical Relief Committee of America in 1944. Dr Allison was departing for the Minter Hospital in Bulsar, India (courtesy New York Academy of Medicine).

services first to the construction workers building the fair in Flushing and then to the visitors and workers once the fair opened.²³ Six first aid stations were built and eventually Hoguet directed the activities of 30 physicians and 40 nurses who staffed the fair. Hoguet's medical operation had five ambulances and a speed boat at its disposal and included a mobile x-ray unit. Hoguet designed the latter with C. I. Headland, MD, after he realized that it would prove too expensive to install x-ray equipment in all of the first aid field stations.²⁴

One of this writer's uncles who worked as a physician at the fair and who was a 1930 graduate of Cornell University Medical College recalled the following in later years:²⁵

Hoguet was an efficient administrator and organizer. He employed large numbers of physicians and nurses at several first aid stations. We physicians worked brief shifts of a few hours each week. Hoguet, however, was on duty all the time and worked very hard to see that everything was functioning alright. Those of us who had known him for years were delighted that he had been appointed the Medical Director of the World's Fair. He was well qualified for the job. It was wonderful to see him immersed again in the medical profession and he seemed happier to me than at any other time since his accident.

FINAL YEARS

The New York World's Fair opened on April 30, 1939, and continued through 1940. In April 1941, Whalen became the chairman of the board of Coty, a cosmetics manufacturer and resumed his role as New York City's official greeter. Hoguet, who had directed medical services at the fair for almost four years, started a private x-ray practice once the fair closed, drawing on his experience with the mobile unit he had helped to develop. At the same time, he became president of a non-profit medical insurance group, the Medical Guild Foundation. Both initiatives were adversely affected by the domestic physician manpower shortages created when the US entered World War II. They eventually had to be abandoned.^{2,20}

In 1942, Hoguet became national director of the Medical and Surgical Relief Committee of America, a position he held until his death (Fig 2). This group provided ambu-

lances and medical kits to Army and Navy units and to foreign relief agencies.²⁶ He also served for a time as a medical consultant to the Republic Aviation Company.

In 1946, Hoguet's health began to fail when he developed symptoms of coronary artery disease. He was admitted to the New York Hospital, where for so many years he had taught Cornell University Medical College students, and died there of an acute myocardial infarction on June 17, at the age of 63 years.^{2,27}

His funeral took place two days later, on June 19, at St Vincent Ferrer Church in Manhattan, and he was interred in Holy Rood Cemetery in Westbury, Long Island. He was survived by his wife of 30 years, Helen, and his four children, Lawrence, Mrs George Helmer, Roland, and J. Peter. His wife died on November 20, 1955.²⁸

Joseph Peter Hoguet bore his unusual success with great modesty and mustered enormous personal and professional courage to meet a devastating tragedy. Those who knew him remember him most today as a modest, generous, kind, and above all as a courageous man who never lost heart in the face of great adversity.

Acknowledgments. I first heard of Dr Joseph Peter Hoguet when I was a young boy. He was a friend and colleague to two of my late uncles who were physicians. They had trained at Cornell University Medical College and the New York Hospital and had assisted Hoguet at surgery. It was because of their admiration for him that I became interested in his professional life. I want to thank Dr Hoguet's son, J. Peter Hoguet, who greatly assisted me in the research process and who offered encouragement. I am also grateful to Dr Bernard J. Pisani, Director Emeritus of the Department of Obstetrics and Gynecology at St Vincent's Hospital and Medical Center and a former president of the Medical Society of the State of New York, who knew Dr Hoguet and who encouraged me to carry this project to completion. I want to thank Ella Abney, Librarian of the Albion O. Bernstein Library of the Medical Society of the State of New York, for her valuable assistance in locating important documents and Dr Hoguet's original medical publications. The New York Academy of Medicine library kindly furnished a photograph from their collection and helped in finding several publications. Michael Raines, Curatorial Assistant, Harvard University Archives, provided me with valuable biographical information for which I am very appreciative. Eleanora Golobic, Archivist at the American Field Service Archives and Museum, furnished valuable information about the American Ambulance Hospital and Dr Hoguet's service there. I want to thank Martin Collins, Archivist, Columbia University College of Physicians and Surgeons and Odile Duff of the American Society of the French Legion of Honor for their assistance. I am very thankful to Maureen Maher for her careful preparation of the typescript.

REFERENCES

1. Personal communication, Bernard J. Pisani, MD, July 8, 1992.
2. Dr J. Peter Hoguet, Surgeon, 63, Dead. *New York Times* June 18, 1946, p25.
3. Personal communication, J. Peter Hoguet, October 20, 1992.
4. Joseph Pierre Hoguet in *Harvard Class of 1904. Twenty-Fifth Anniversary Report*. Norwood, MA. Privately printed for the class by the Plimpton Press, June, 1929, pp362-364.
5. Robert Louis Hoguet, in *Who Was Who In America* Volume IV 1961-1968, Chicago, Marquis Who's Who Inc, 1968, p451.
6. Letter from J. Peter Hoguet to Pascal James Imperato, MD, September 30, 1992.
7. Joseph Peter Hoguet. *JAMA* 1946; 132:39.
8. Joseph Augustus Blake. *JAMA* 1937; 109:726.
9. Dr Joseph Augustus Blake. *American Men of Science. A Biographical Directory*. Garrison, NY, The Science Press, 1921, p65.
10. William Bradley Coley, MD, in Walsh JJ, *History Of Medicine in New York. Three Centuries of Medical Progress*. Volume V, New York, National Americana Society, Inc, 1919, pp241-243.
11. William Bradley Coley. *JAMA* 1936; 106:1155.
12. Coley WB, Hoguet JP: Melanotic cancer. *Ann Surg* 1916; 64:206-241.
13. Coley WB, Hoguet JP: Operative treatment of hernia. *Ann Surg* 1918; 69:255-268.
14. Hoguet JP: Direct inguinal hernia. *Ann Surg* 1920; 72:671-674.

15. Hoguet JP: Observations on two thousand four hundred and sixty-eight hernia operations by one operator. *Surg Gynecol Obstet* 1923; 37:71-75.
16. Personal communications, P. J. Imperato, MD, 1940s-1960s.
17. Hoguet JP: Reconstruction of hip-joint disorganized by Charcot's Disease. *Ann Surg* 1926; 83:693-695.
18. Hoguet JP: The use of fascia as suture material. *Amer J Surg* 1929; 6: 812-813.
19. Personal communication, James A. Imperato, 1950s.
20. Letter from J. Peter Hoguet to Pascal James Imperato, MD, November 4, 1992.
21. Beekman F: *Hospital for the Ruptured and Crippled. A Historical Sketch Written on the Occasion of the Seventy-Fifth Anniversary of the Hospital*. New York, privately printed, 1939, p127.
22. Grover Aloysius Whalen, in Garraty JA (ed), *Dictionary of American Biography*. supplement seven, 1961-1965, New York, Charles Scribner's Sons, 1981, pp779-781.
23. Personal communications, Louis G. Imperato, Esq, 1992.
24. Hoguet JP, Mazet R, Jr: Mobile roentgen-ray unit used at the New York World's Fair. *AJR* 1941; 45:124-126.
25. Personal communication, Alfred A. Imperato, MD, 1988.
26. *Committee Report of the Medical and Surgical Relief Committee of America*, 7(12), 1946.
27. Joseph Peter Hoguet, in *Harvard Class of 1904. Fiftieth Anniversary Report*. (Eleventh Report), Cambridge, MA, Printed for the Class of 1904 by the Harvard University Printing Office, June 1954, p220.
28. Mrs J. Peter Hoguet. *NY Times* November 23, 1955, p23.

Medical spoons

A brief look at patents of the 1870s and 1880s

JOHN S. HALLER, JR, PhD

Standing on the threshold of the 20th century, and looking back 100 years, the 19th century presents in the field of invention a magnificent museum of thoughts crystallized and made immortal, not as passive gems of nature, but as potent, active, useful agencies of man. (Edward W. Byrn, *The Progress of Invention in the Nineteenth Century*, 1900)

"Technology," wrote William F. Ogburn in *Technology and Social Change* (1957), "is like a great mountain peak. It looks different according to the side from which one views its."^{1(p3)} Clearly, many have interpreted or appreciated technology simply at the level of gadgetry, with 100s if not 1,000s of the inventions placed at society's disposal through aggressive advertising. Others have understood technology as a precursor to unemployment through increased efficiency and the gradual replacement of jobs; the destroyer of artistic skills and natural resources; the engine of material wealth and power for both individuals and nations; the instigator for greater secularization (versus spiritualization) of society; a catalyst of change; a polluter of the environment; and a perpetrator of socio-economic imbalances between people and nations. Actually, technology has been all these things and more.

PATENTS AND PATENT LAW

To look at the 1870s and 1880s in America is to observe a period bristling with all types and ideas about mechanical devices—a reflection of the country's belief that it had the industrial future by the tail and the products of Yankee ingenuity would soon fill the corners of the earth. The number of patents approved by the Patent Office of the United States Department of Commerce seemed to grow exponentially with American expectations. In the area of invention, many historians and social scientists have viewed the 19th century as unique among centuries. Edward F. Byrn, author of *The Progress of Invention in the Nineteenth Century* (1900), proudly characterized his age as a "gigantic tidal wave of human ingenuity and resource."^{2(p3)} At the approach of the century, the world of invention witnessed

James Watt's steam engine and Eli Whitney's cotton gin. However, genius such as theirs still struggled to overcome bigoted prejudice, especially when many craftspeople opposed labor-saving machinery as a threat to the future livelihood of the working classes.

In spite of the working-man's initial opposition, by the end of the century, the United States led the world in labor-saving devices, including 445,064 miles of railway track and enough rolling stock to make continuous trains stretching three times across the continent from the Atlantic to the Pacific.^{2(p5)} It was a century of milestones in inventions from the telephone, phonograph, and graphophone, to cable-cars, electric railways, electric lights, the telegraph, sewing machines, reapers, india-rubber goods, cameras, gas engines, cash registers, Gatling guns, linotype machines, sanitary plumbing, air brakes, coal tar dyes, dynamite, aluminum ware, Bessemer steel, enameled iron ware, tin-can machines, cigarette machines, fountain pens, knitting machines, oleomargarine, friction matches, x-ray apparatus, and moving pictures.

The stimulus for this creativity was a patent law that regarded the inventor as a public benefactor and sought to protect for him whatever riches accrued from his invention. Following separation from England, the states under the Articles of the Confederation granted both special monopolies to protect manufacturing and industry, and patents to encourage and protect new inventions. Not until 1790, following the establishment of the federal system of government, did Congress remove this power from the states by passing a federal patent law designed to promote the "progress of science and the useful arts by securing for limited times to authors and inventors, the exclusive rights to their respective writings and discoveries."³ A second patent law in 1793 registered patents without examining their originality. The repeal of this registration system in 1836 provided for the close examination of each patent application. This act also created the United States Patent Office, whose commissioner of patents was given the authority to examine the validity of each application. Under the 1790 and 1793 patent laws, inventors filed some 9,957 patents. From 1836 until 1900, inventors filed 650,123 patents.^{2(pp13-19,463,464)}

From the Department of History and Medical Humanities, Southern Illinois University at Carbondale, Carbondale, IL.

Address correspondence to Dr Haller, Professor of History and Medical Humanities, Southern Illinois University at Carbondale, Colyer Hall, Carbondale, IL 62901.

MEDICAL PATENTS

Stanley Joel Reiser in his *Medicine and the Reign of Technology* (1978), argues persuasively that physicians moved through three distinct stages in their diagnostic relationship with patients. First, physicians relied on a "verbal technique of information gathering," followed by "direct connection with their patients' bodies through techniques of physical examination," to finally "indirect connection with both the experiences and bodies of their patients through machines and technical experts." In looking at the signposts for this evolution, from the collection of symptoms from the patient's personal description of an illness and the physician's observations, to the use of the stethoscope, to finally the reliance upon knowledge derived from the laboratory, clearly Reiser's analysis bears scrutiny.⁵(p227)

What Reiser's analysis did not account for was the plethora of inventions that developed in response to the American penchant for self-dosage. This aspect of health care, which has continued unabated into the present with thousands of over-the-counter medicines, reached significantly alarming proportions in the second half of the 19th century with the marketing and sale of patent and proprietary medicines. Much has been written about this period of laissez-faire pharmacy; books detail the fraudulent claims of these medicines, their high alcoholic and opium content, and the history of their poisonous or addictive effects.

In the decades before the passage of the Pure Food and Drug Act of 1906, traffic in these medicines knew few bounds. Proprietary medicines such as Warner's Safe Cure, Scott's Emulsion, Ayer's Sarsaparilla, Hamlin's Wizard Oil, Puritana, Hale's Honey of Horehound and Tar, Electric Bitters, Peruna, Horsford's Acid Phosphate, and 100s of others, were sold in abundance from pharmacy shelves. Designed to respond to the self-dosing tendencies of the American public, these medicines offered the promise of vigorous health and a quick and cheap remedy for life's miseries and diseases. By searching the shelves of the nearest drugstore, asking across-the-counter advice from pharmacists eager to sell merchandise, or explaining one's symptoms in writing to a so-called doctor who manufactured and sold medicines, America's self-reliant sick could purchase health without paying for a physician's visit and prescription.

MEDICAL SPOONS

Over a period of 20 years, from 1870 until 1890, approximately a dozen medical spoons were patented for manufacture and distribution. Their existence, in many ways, reflects this laissez-faire episode in medicine and pharmacy when newspapers and magazines advertised a bizarre assortment of pills, powders, tonics, extracts, infusions, elixirs, healing herbs, and other sure cures for America's sick. This was also an age of home remedies, concocted from a combination of folklore, homemade science, empiricism, and superstition. It was a period when patient credulity matched evenly the marketing abilities of a rag-tag band of drug manufacturers willing to bottle anything that might sell.

Interestingly, the descriptions accompanying these patents did not imply their purchase or use by physicians. The words "doctor" and "physician" were conspicuously absent from the descriptive account accompanying the patent narrative. Instead, medical spoons were intended princi-

pally for the parent or self-doser without reference to the family doctor. The medical spoons patented during this brief period were generally of three types: a combination spoon-cover and spoon-holder, a non-spill spoon, and a pocket-size spoon for easy transportation.

The combination spoon-cover and spoon-holder, patented between 1879 and 1886, was designed to contain the medicine and, simultaneously, provide a stable, non-spill, platform for resting the spoon on a table. Sometimes called the "mustache-spoon" because of its peculiar sliding lid over the bowl to prevent facial hair from touching the medicine, it represented the more complicated of the patented devices. The patented medicine spoon of Barclay T. Trueblood of Handley, Indiana, consisted of a combination spoon/cover which fitted over the bowl (Fig 1). The appeal of this particular spoon was that it could be set on a flat surface without danger of the contents spilling out. In addition, Trueblood designed the bowl with a cover and a small cover handle, which laid over the larger spoon handle. When medicine was placed in the spoon and the cover placed over it, the user could bring it to his own or the patient's mouth without spillage. This was particularly important when administering medicines to infants, the elderly or infirm whose hands were unsteady, those who resisted medication, or those in a recumbent position who worried about spillage. Essentially, the design allowed the user to insert the spoon between the lips and teeth before pressing on the handle cover to open the lid and allow the medicine to run down the patient's throat.⁶

A variation of the Trueblood design was the medicine spoon of Thomas M. Baker of Washington, DC, patented in 1880. This spoon had many of the same attributes as Trueblood's device, including the ability to stand without spillage (Fig 2). The difference between the two was Baker's spring-mounted cover and V-shaped attachment on the curve of the spoon bowl, the latter of which made it difficult to insert the spoon too far into the patient's mouth. Baker claimed that the advantages of his invention were that it allowed the spoon to be easily filled with the desired quantity of medicine, that the spring-mounted cover prevented the patient from seeing or smelling the medicine, and that the spoon could be set down without spillage.⁷

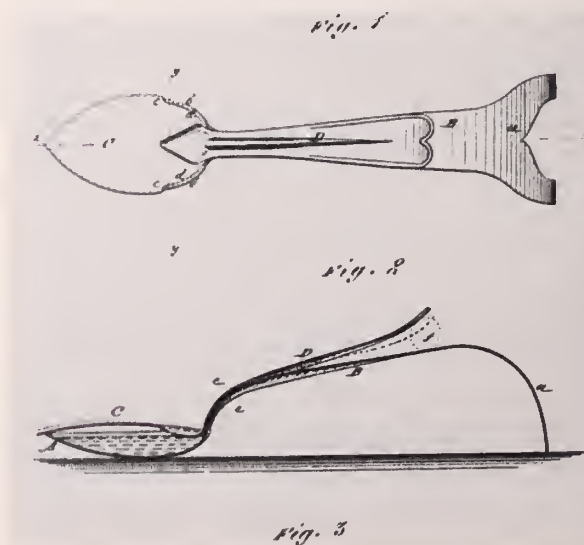


FIGURE 1. The Trueblood spoon.

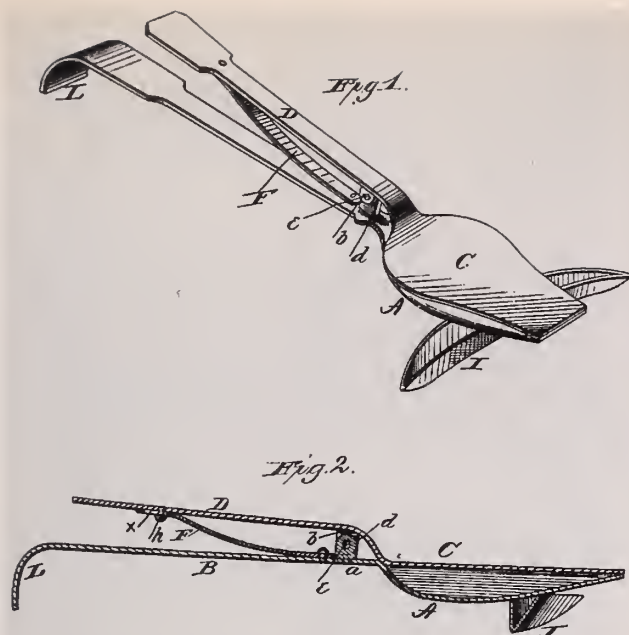


FIGURE 2. The Baker spoon.

A third variation on this design was patented in 1883 by Mrs Sophia Pelkey of Eau Claire, Wisconsin and called the medical spoon and vial holder (Fig 3). Like the Baker model, it could be placed on a table without spillage and had a spring-mounted cover that dispensed precise amounts of medicine to the patient while concealing its contents in a box-type container in the spoon stem. What differentiated the Pelkey spoon from the former two models was the

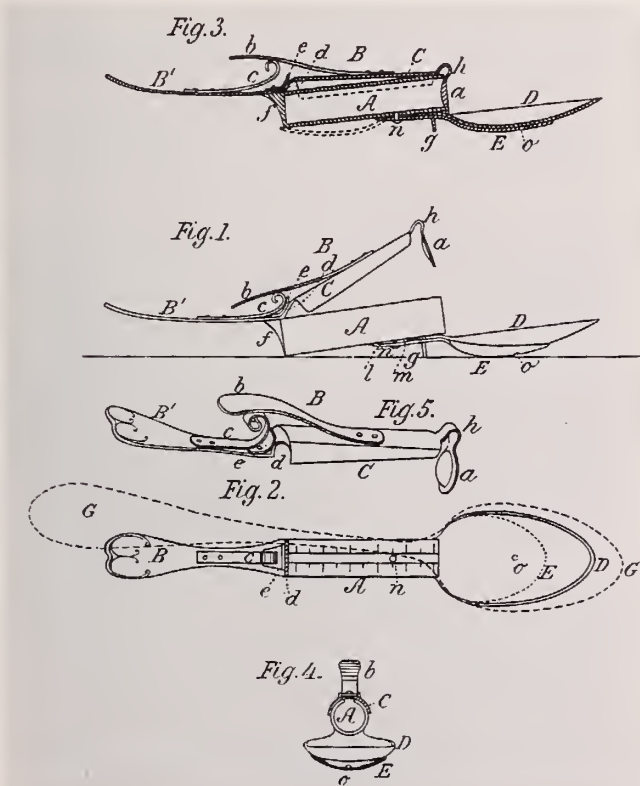


FIGURE 3. The Pelkey spoon.

ability of the user to stop or control the flow of the medicine to the bowl by means of its spring-mounted cover.⁸

A second type of medical spoon, more simplified in design from the spring-mounted cover, and patented between 1879 and 1886, was also intended by its inventors to prevent spillage. Safe compartments within the spoon handle and a continuous flange around the bowl characterized this design. The 1879 nursery and medical spoon of John W. Force of Springfield, Massachusetts, was typical of this design. The device had the look and weight of most spoons except that the bowl of the spoon had a covering soldered around its edges (Fig 4). At the back end of the convex cover was a small opening into which the user poured the medicine. A smaller opening at the tip of the bowl, ideal for babies and others who were difficult to nurse, allowed the medicine to exit into the patient's mouth without spillage.⁹

The medical and nursery spoon patented in 1881 by Herbert Clayton of Cincinnati, Ohio, was of similar design. It consisted of a porcelain spoon with a removable metal cover, which was sprung into position (Fig 5). A wire running the full length of the stem strengthened the porcelain handle. Unlike the Force design, the stem turned downward to provide support when placed on a table. Like the invention of John Force, however, the cover had two openings, one to receive the medicine and another to dispense it in the patient's mouth. Unlike the Force spoon with its soldered top, the cover of the Clayton spoon was detachable, neatly fitting into the inner sides of the grooved bowl. This allowed the owner to remove the top for better cleaning.¹⁰

Conrad S. Dorr of Wheeling, West Virginia, patented a medicine spoon in 1886, which while similar in appearance to the Clayton spoon, was actually the most radical of the spoon designs, at least in terms of its purpose. Because many patent and proprietary medicines contained corrosive acids that harmed the teeth, Dorr intended his spoon to permit delivery of the fluid without otherwise harming the

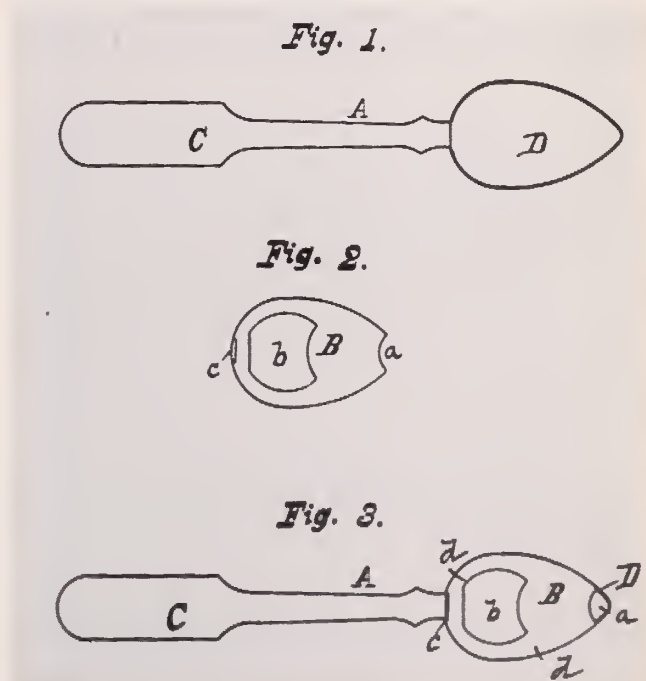


FIGURE 4. The Force spoon.

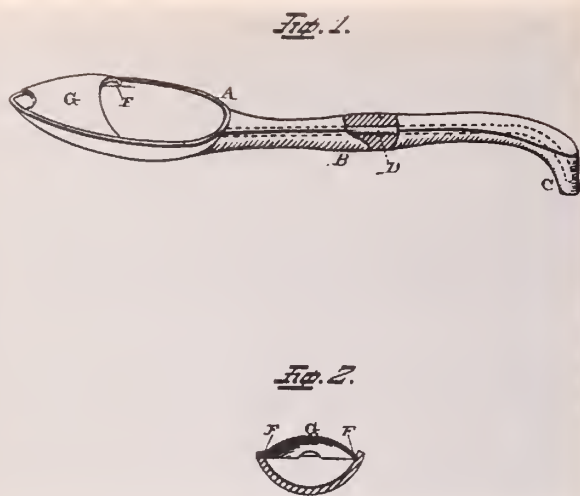


FIGURE 5. The Clayton spoon.

teeth. The bowl of the spoon was gourd-shaped, made of glass, with graduated measurements on the side for easy reading (Fig 6). Unlike other medicine spoons, however, it had a hollow handle open at both ends. After the liquid was measured in the bowl to ensure an accurate dosage, the spoon was turned around and the handle of the device was inserted into the back of the mouth to carry the liquid to the throat without contacting the patient's teeth. According to Dorr, this allowed individuals to take harsh medicines without damaging their teeth or leaving a disagreeable taste in the mouth.¹¹

The device patented in 1886 by William H. Welsh of York, Pennsylvania, consisted of a graduated spoon whose extra-wide stem provided a stable platform when placed on a table. The bowl had corrugations or ribs, marking varying dosages from a half teaspoon to a tablespoon (Fig 7). By filling the bowl to the top of a specific rib, the user ensured an exact dosage. Welsh recommended the use of glass, porcelain, or metal for his spoon and guaranteed that it required neither skill nor art to use it.¹²

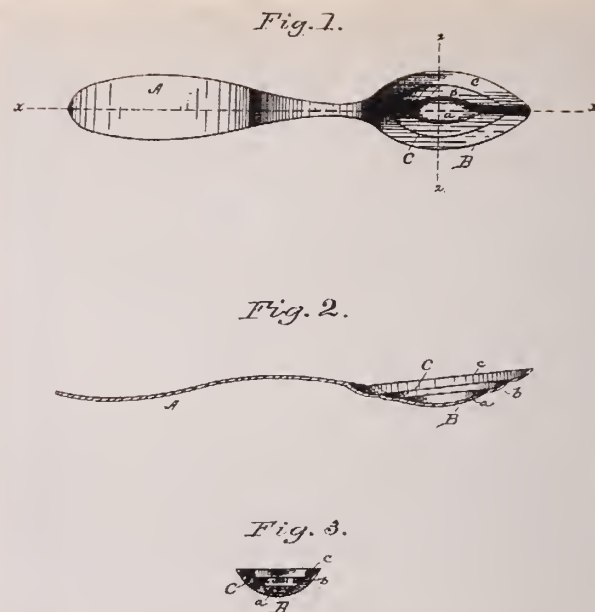


FIGURE 7. The Welsh spoon.

Finally, there was the unusual medicine spoon patented by Elisabeth Guyon of New York City in 1877 designed for the administration of both liquid and powdered medicines. Its unusual length served multiple purposes (Fig 8). The back of the handle twisted to form a spiral and provided an effective stirring surface when inserted into a medicine bottle or package. In addition, the stem acted as a chisel-shaped scraper to break up coagulated or lumpy masses, or to scrape medicines adhering to the interior surfaces of a bottle. The fluted middle portion of the stem served to channel medicines from the sides of a bottle into the graduated bowl.¹³

A third type of medicine spoon, small and compact, was designed for convenience and ease in carrying. Frank H. Wyeth of Philadelphia patented a spoon in 1886 that when not in use, snapped into a metal or hard rubber cap for easy transport (Fig 9). Although obviously applicable to the physician who wanted an easily portable spoon when he visited patients, it more effectively served the needs of the self-dosing patient who carried his bitters or tonic and

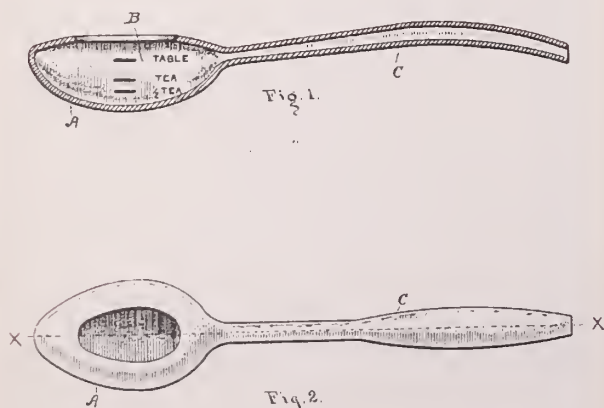


FIGURE 6. The Dorr spoon.

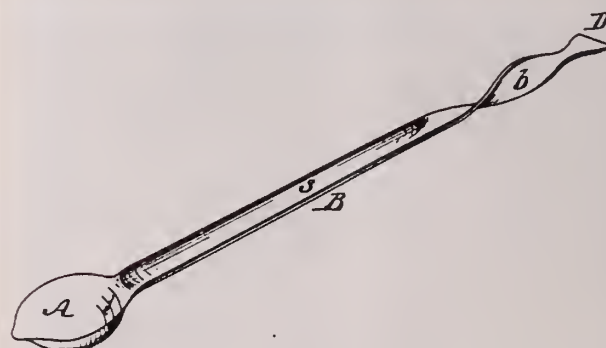


FIGURE 8. The Guyon spoon.

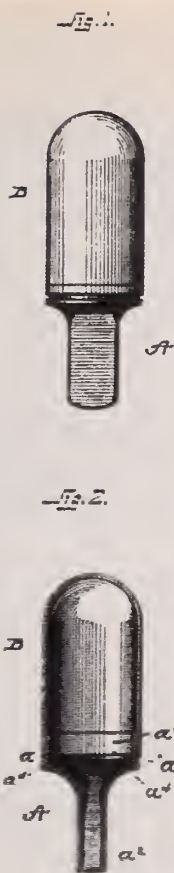


FIGURE 9. The Wyeth spoon.

needed a spoon that fit comfortably into a handbag or vest pocket.¹⁴

Another variation designed by Boise Sherwin of New York City and patented in 1886 packed conveniently in a pocket, purse, or medical bag. The spoon consisted of a wide, shallow bowl; a short, flat handle; and two small legs of equal height soldered to the underside to support the spoon without spillage (Fig 10). The bowl could hold a

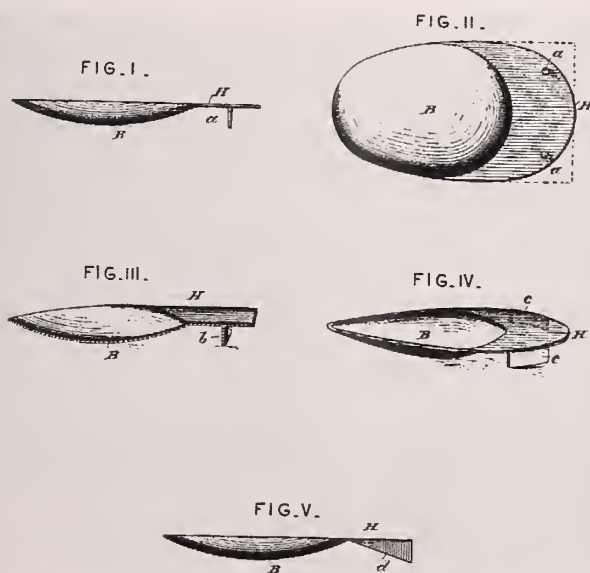


FIGURE 10. The Sherwin spoon.

teaspoon or more of medicine. Sherwin proposed constructing the spoon of glass or other cheap metal. Small, inexpensive, and easily cleanable, the device offered an agreeable alternative to bulky spoons of a more traditional design.¹⁵ Finally, the combined medicine spoon and cork screw designed by William R. Noe of Newark, New Jersey, and patented in 1886, consisted of a spoon with a short shank or stem. At the end of the stem pivoted a corkscrew used for drawing a cork cap from a medicine bottle (Fig 11). Although small, the spoon served as a convenient grasping handle for pulling on the cork.¹⁶

RETROSPECT

To be sure, inventions were not all equal in their effects. While some had an almost immediate impact on society, others were far less obvious, and many were soon forgotten. Surely medical spoons patented in the 1870s and 1880s caused barely a ripple in the stream of inventions pouring from the genius of 19th century Yankee ingenuity. Although patents for medical spoons represented only a small piece of the larger patent phenomena, their existence does help to explain the totality with which American inventors challenged traditional ways of doing things. Even such simple utensils as spoons were subjected to the impact of the century's technological fervor.

If one looks at an individual medical spoon patent, it is difficult to imagine any special significance. However, if one groups the patents, they acquire a distinction not unlike other clusters of medical and pharmaceutical devices in the late 19th century. Like the aggregation of inventions

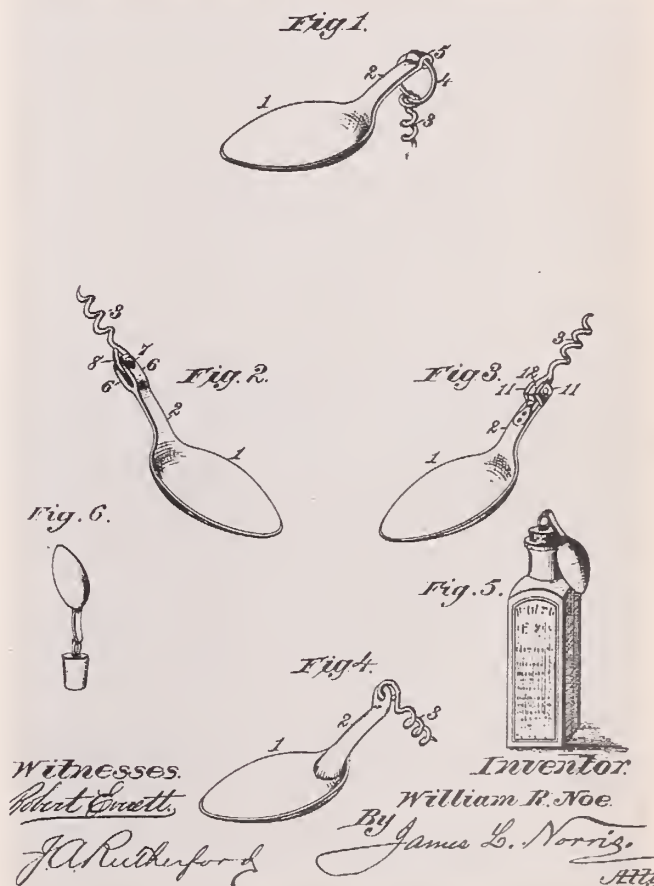


FIGURE 11. The Noe spoon.

spawned around the railroad, the gasoline engine, and the electric motor which stimulated a host of supportive industries, the plethora of medical spoon patents in the 1870s and 1880s provided an added perspective that helps explain the forces, challenges, experiences, leadership, direction, and impact of medical inventiveness in the late 19th century.

Overall, the 20 years from 1870 to 1890 marked the high tide of patent and proprietary medicines in America. Here was an age resplendent in material triumphs and not yet self-conscious of its problems and abuses. America's pharmaceutical industry, one of many that responded to the market opportunities of the post-Civil-War decades, reflected both the promise and the contradictions of the age. Around this industry there developed a large and significant practice of self-dosage built on mass advertising, shrewd and unbridled claims, and an enthusiastic heterodoxy. No one system of medicine predominated as the industry sought to build alliances with every sectarian scheme. In an age of no settled standards, self-dosage and its complement of medical spoons competed aggressively

with orthodox medicine for its share of the health care market.

REFERENCES

1. Ogburn WF: The meaning of technology, in Cuber JF (ed): *Technology and Social Change*. New York, Appleton-Century-Crofts, Inc, 1957.
2. Byrn EW: *The Progress of Invention in the Nineteenth Century*. New York, Russell and Russell, 1970.
3. *United States Constitution*, A1, 8, P8.
4. Vaughan FL: *The United States Patent System*. Norman, University of Oklahoma Press, 1956.
5. Reiser SJ: *Medicine and the Reign of Technology*. London, Cambridge University Press, 1978.
6. Trueblood BT: Medicine-Spoon, US Patent 22,549, December 9, 1879.
7. Banker TM: Medicine-Spoon, US Patent 233,185, October 12, 1880.
8. Pelkey S: Medicine Spoon and Vial Holder, US Patent 277,924, May 22, 1883.
9. Force JW: Nursery and Medical Spoon, US Patent 212,677, February 25, 1879.
10. Clayton H: Medical and Nursery Spoon, US Patent 244,551, July 19, 1881.
11. Dorr CS: Medicine-Spoon, US Patent 353,055, November 23, 1886.
12. Welsh WH: Medical Spoon, US Patent 343,510, June 8, 1886.
13. Guyon E: Medicine-Spoon, US Patent 358,197, February 22, 1877.
14. Wyeth FH: Medicine Holder, US Patent 350,406, October 5, 1886.
15. Sherwin B: Medicine Spoon, US Patent 339,221, April 6, 1886.
16. Noe WR: Medicine Spoon, US Patent 350,499, October 12, 1886.

FROM THE LIBRARY

MEDICAL ERRORS

The erroneous medical notions of the laity were once the accepted views of the medical profession. The popular errors of to-day are the professional errors of our forefathers. For a long time the public cherishes as truth what was once believed and then relinquished by medicine. Medicine is advancing by discarding errors and acquiring new knowledge. The public has not the discernment to discard medical errors, but holds on to them, and they become of service to the charlatan in fastening himself upon the public.

EDITORIAL
(*NY State J Med* 1908; 8:553.)

When death restores life

DOUGLAS M. SENDEROFF, MD

As I gaze upon the rainswept runway from the comfort and security of the pilots' lounge at Teterboro Airport, I am filled with a sense of adventure and purpose. In 60 minutes, I and two fellow members of the transplant team from Mt Sinai Hospital in New York City will depart for Florida to harvest a liver for an urgent transplant operation. Meanwhile, back at Mt Sinai, my co-resident is carefully reviewing the preoperative laboratory status of our chosen recipient. "We have a donor in Florida," the hopeful surgical resident enthusiastically proclaims as he enters his patient's room. Lean and hungry and wearing rumpled surgical greens and a two-day old beard, he withdraws his prized Mont Blanc pen, a graduation gift from his proud parents, from his shirt pocket. "Orthotopic liver transplant with venous bypass" reads the informed consent. The patient, a 42-year-old woman suffering from the effects of end-stage liver disease, does not hesitate as she tearfully signs for the operation for which she has waited months. She has already received passing grades from her internist and the 30 member panel of the recipient selection committee of Mt Sinai consisting of surgeons, gastroenterologists, psychiatrists, and social workers. Tomorrow, she will become one of the 2,000 patients who undergo liver transplantation each year in the United States.

Almost 30 years have passed since Thomas Starzl attempted the first human orthotopic liver transplant at the University of Colorado. Before the advent of cyclosporine in the 1980s, the role of liver transplantation was questionable. In the past decade, however, the results of hepatic transplant have improved to the point that present one year survival figures are above 80% at many centers. In addition, the five year mortality rate is less than 5% after the first post-transplant year in most reported series.

The cabin is small, but my leather captain's chair is very comfortable as I observe the pilot skillfully work the instrument panel of our Lear jet. At 30,000 feet and 450 mph, the terror of a turbulent takeoff has passed. I am of eager mind but of uneasy stomach as the veteran surgeons feast on fresh fruit and cheese. This plane is built for speed, not comfort. There is no bathroom. The glamour of being a flying surgeon has somewhat diminished.

The cost of a single liver transplant is \$125,000 with \$10,000 in yearly follow-up expenses. How can a life be assigned a monetary value, I ponder. The future of medicine is in high-technology, high-profile procedures, I assure myself. Could this money be more economically spent on preventive medicine and community health projects, I query. Would a socialized system of health-care delivery

view this expensive undertaking as a necessity or as a drain of resources? Let us not forget the human cost of injury to trained health professionals involved in misadventures of the air and highways.

Stepping onto the runway in Florida, I remove my winter armor and rejoice in the balmy tropical air reminiscent of carefree vacations and long summer nights. I am quickly reminded of our task as the ambulance unveiled in the evening mist approaches our plane, ready to transport us and our vital equipment to the hospital.

Accompanied by a life-support system, the organ donor arrives in the operating room where she is reconnected to the respirator. Although her young heart is beating defiantly, she is brain dead, a legally and medically definable state, synonymous with the death of a human being in the United States. Her premature demise came suddenly, the swift result of a ruptured blood vessel in the brain. Contemplating the tragic events that have brought us together I silently lament while attempting to remain impassive.

As I initiate the familiar ritual of the five minute preoperative scrub, I rehearse my role in the performance about to commence. Entering the operating theater, I become secure in an environment which has become comfortable to me over the past several years. Under the bright overhead lights my concentration is focused as surgery begins. A dramatic midline thoracic and abdominal incision is made to provide full exposure of the liver and its vascular structures. Our team works silently and meticulously fully aware that any injury to the liver during our operation may lead to complications later on. The scrub nurse is well rehearsed and supports us in our leading roles, efficiently filling our hands with the instruments we need. After one hour, the liver is separated from its lifeless owner and readied for transport. The role of the donor is over after having supplied us with our precious cargo. Triumphant, we retreat to the airport with our immortal treasure secure in its icy chest.

Touching down at 7 AM, we are just in time to battle the New York City rush hour traffic. The police, alerted to the urgency of the situation, escort us on a wild trek across the George Washington Bridge and through the congestion of the FDR Drive. With cooler in hand, I burst through the Mt Sinai emergency room entrance proudly bearing the product of our nocturnal expedition. On reaching the operating room, I join the remaining members of the transplant team who are rested and ready for the 8-12 hour recipient operation.

The chief surgeon of the transplant service is optimistic and confident in his ability to perform one of the most challenging procedures in general surgery requiring both vascular and hepatobiliary expertise. As the captain of the

From the Department of Surgery, Beth Israel Medical Center, New York, NY.
Address correspondence to Dr Senderoff, 353 East 17th St, 12G, New York, NY 10003.

ship, he is responsible for coordinating the efforts of his crew including three gowned and gloved junior officers who await his command. After many tedious hours, the vascular anastomoses are completed, and we cautiously release the clamps. Immediately after recirculation, the seas turn stormy as blood fills the surgical field. The room grows silent except for the beeping of the anesthesia monitors. The source of hemodynamic instability is identified as a gaping hole in the suture line of the vena cava and is finally controlled with a series of well-placed stitches. Our anesthesia team keeps us afloat by maintaining adequate cardiac output, allowing us to maneuver out of uncharted waters. After hemostasis is completed and the biliary anastomosis is created, drains are placed in preparation for the completion of our journey. We are now sailing in smooth waters and our captain is pleased at the forecast. Only 10 of the 65 units of packed cells reserved for us at the blood bank have been transfused. Attached to its new blood supply, the liver is pink and appears to be thriving. Filled with a sense of accomplishment, we steer toward home.

Following closure of the Mercedes incision, a permanent insignia of her identity as a transplant recipient, our patient is escorted directly to the Surgical Intensive Care Unit where she will be closely monitored for several critical days. Approximately 70% of recipients experience at least one episode of rejection after liver transplantation. Our patient will have to follow a strict regimen of immunosuppressive drugs that will render her vulnerable to a variety of virulent pathogens. In addition, biliary obstruction and hepatic artery thrombosis may occur later in the postoperative course. Follow-up sonograms, cholangiograms, liver biopsies, and blood tests will predominate her new life as a liver transplant recipient. Only she can judge the quality of her renewed existence.

As the triumphant transplant team begins to disperse, I am both exhilarated and exhausted by the drama of the past 24 hours. Lying in a meditative state in my darkened on-call room, my body hungers for sleep. I am restless, however. My mind has been aroused from its slumber, my soul inspired, awakened by the modern medical miracle that has enabled one person's death to restore another's life.

Home care

Doing right for the wrong reason

ALLEN D. SPIEGEL, PhD

Increasingly, physicians and other health-care providers are participating in the delivery of medical and health-care services to patients in their homes.¹ Frequently, the terms "home-health care" and "home care" are used synonymously. From a personal viewpoint, the two terms reflect a major philosophical difference that directly influences the role of the physician and the quantity and quality of care rendered. In general, home health care tends to concentrate on services in the medical/health spectrum. On the other hand, home care is a comprehensive approach that combines social/personal services with medical/health needs.

MEDICAL INVOLVEMENT IN HOME CARE

Illustrative of the surge in organized medicine's involvement in home care, the recently established American Academy of Home Care Physicians currently has about 550 members and is rapidly growing. Dr Joanne Schwartzberg, the American Medical Association's (AMA) Director of the Department of Geriatric Health, is the President-elect of that organization. In addition, a Home Health Care Society has been proposed by the American College of Physician Executives.²

This increasing interest in home care is linked to cost containment of health-care services. That cost containment push was the immediate rationale for the imposition of the

federal government's prospective payment system (PPS) that initiated the diagnosis related groups (DRGs) reimbursement mechanism in October 1983.³

PHYSICIAN AWARENESS ABOUT HOME CARE

Even before the PPS/DRG began, the Medical Society of the State of New York advocated physician awareness about home-health care. As early as 1978, Weller⁴ described the following six elements of the physician's role in home-health care in an article published in the *Journal*: knowing what home care is available in the area; understanding the mechanics of referral to home-care services; coordinating home care in the community; maintaining the reports and keeping clinical records on each patient; helping establish coordinator positions to manage each patient; and being aware of reimbursement alternatives for payment.

Adding another aspect to the physician's role, Driscoll⁵ observed that house calls were a medical tradition from the time of Hippocrates. A home-care visit helped the physician to make a diagnosis as elaborated by the mnemonic HOUSE: House (look at dwelling, entry, neatness, pictures); Others (Who else lives there? How do they interact?); Uncover (look for problems, discover new information); Supports (identify needed support services such as visiting nurse); Emergencies (Telephone available with vital numbers listed? Is there an automated emergency call system?).

Experts urged physicians not to forfeit their role to service agencies in the burgeoning arena of home care.⁶ An editorial in *American Medical News*⁷ also advocated expand-

From the Department of Preventive Medicine and Community Health, State University of New York, Health Science Center at Brooklyn, Brooklyn, NY.

Address correspondence to Dr Spiegel, Department of Preventive Medicine and Community Health, State University of New York, Health Science Center at Brooklyn, 450 Clarkson Avenue, Brooklyn, NY 11203.

ing the leadership function of physicians in home health care.

DEFINING A PHYSICIAN'S ROLE IN HOME CARE

Crucial to a comprehensive approach to home care, the physician is still the legal "captain of the ship." The physician is responsible for making the medical diagnosis, preparation of the treatment plan, ordering ancillary personnel care, and the prescribing of equipment and supplies for the care of the patient in the home. Without the physician's order, home-care services will not be reimbursed by insurers.

An AMA⁸ definition states that home care is "...the provision of equipment and services to the patient in the home for the purpose of restoring and maintaining his or her maximal level of comfort, function, and health." Function is a key word in this explanation. Ramifications of that AMA definition are reinforced in the AMA publication, *A Physician Guide to Home Health Care*, first published in 1979 and completely revised in a 1989 edition. This booklet addresses issues such as the use of home-care services, insurance coverage, payment for services, and physician management in home care. Commenting that the Health Insurance Association of America urges its members to "...make homecare insurance benefits available under their medical expense policies," the guide included model state legislation to do exactly that. That sample law detailed definitions, number of visits, deductibles, coinsurance, and applications to short-term policies. A typical physician home-care treatment plan illustrated entries on skilled nursing care, occupational therapy, progress notes, and an addenda to the plan. Stressing the physician's pivotal therapeutic role, the AMA guide states, "Appropriate physician participation and leadership is indispensable to the delivery of high-quality home health care. . . . When there is insufficient participation, the quality of care may suffer."

REIMBURSEMENT FOR HOME-CARE SERVICES

Keeping the home-health care and home-care distinctions in mind, Medicare and Medicaid usually reimburse for home health care. Organizations concerned with the aged, social service agencies, and charitable organizations remunerate for home care. Spiegel⁹(pp38-48) identifies and describes the reimbursement proclivities of the major federal governmental economic players: Medicare, Medicaid, Older Americans Act, and the Social Services Block Grant of the Social Security Act. Home-care services may also be funded by commercial insurance companies, Blue Cross plans, prepaid group health plans, voluntary non-profit health and/or disease oriented agencies, United Way agencies, and a variety of organizations sponsored by religious groups.

HOME CARE IN THE PROFESSIONAL LITERATURE

The professional literature also reflects the growth of interest by health-care providers. A 1980 Medline computer search of the medical and health literature revealed more than 100 articles detailing the scope of home-care activities, addressing issues such as Alzheimer's disease, home birthing, hospice, and vascular surgery aftercare.¹⁰(pp59-72) In 1991, more than 700 articles were cited under home-care services, home nursing, home care, and hospices. In the first three months of 1992, more than

200 items were cited including articles on the acquired immunodeficiency syndrome (AIDS) and home care.

In spite of the substantial increase in professional literature, the level of physician awareness is still not as high as it should be. For example, as late as November 1991, Rogatz, Schwartz, and Dennis¹¹ commented that "professionals don't understand how hospice works." Earlier that year, Koska¹² discussed how to stimulate physician leadership and participation in home care.

MEETING THE NEED FOR HOME CARE

A November 1991 survey reported that almost 6% of American households, millions of families, used home health-care services.¹³ More than 5 million people over aged 45 years need help with both physical and household activities. To compound the problem, by the year 2050, one of four Americans will attain the age of 65. Furthermore, the number of Americans over 85 years of age will double, to compose about 20% of the population.¹⁴ This older population will require more health care and use more resources.

Feller¹⁵(p89) indicates that 337,000 children, aged 6-17 years, need functional assistance with activities of daily living such as eating, bathing, dressing, toileting, and mobility. About 10%-15% of children have a chronic health condition, and one million of those have a severe form of that condition. A 1989 Government Accounting Office (GAO) study¹⁶ of the home-care experiences of almost 900 parents of chronically ill children found that 98% had no problem securing medical services. In contrast, parents did have considerable difficulty securing support services due to limited insurance coverage, a lack of information, and no focal contact point. Additionally, about one million young adults, aged 18-44 years, need similar ADL help plus aid with shopping, meal preparation, money management, leisure activities, and household chores.

Technological advances now allow a mini-hospital to be set up in the home. Innovations include the following: infusions for total parenteral nutrition, enteral nutrition, chemotherapy, antibiotic therapy, fluid replacement, and pain control; respiratory service including oxygen therapy and mechanical ventilation; dialysis, continuous ambulatory peritoneal dialysis; insulin therapy using computer-controlled ambulatory pumps and devices; medical equipment such as portable cardiac defibrillators and rehabilitation devices. Virtually every treatment available in the hospital can be provided in the home.

Marketing the rental, sales and service of durable medical equipment is a profitable business. Physicians may be solicited by aggressive salespersons to prescribe an array of devices and equipment. Under that type of sales pressure, fraud and abuse can be a problem.¹⁷ Pierre¹⁸ has recommended national guidelines to assist health-care professionals unfamiliar with home care. Physicians are required to sign a "certificate of medical necessity" for reimbursement by Medicare and Medicaid.

Indicative of the scope of home care, services may be provided by a variety of personnel: audiologists, housekeepers, clergy, construction workers, dentists, visitors, home health aides, homemakers, laboratory technicians, licensed practical nurses, meals-on-wheels delivery people, nutritionists, occupational, physical, and speech therapists, optometrists, personal care assistants, pharmacists, physicians, podiatrists, psychologists, registered nurses, respiratory

therapists, social workers, telephone visitors, vocational and educational rehabilitation specialists, and volunteers. In many cases, family members act as caregivers providing the bulk of home-care services while suffering the exhausting emotional and physical burden. Respite services can be arranged, with either a short-term stay in an institution or temporary help in the home.

Physicians must receive reports from all providers of home care and must coordinate the patient's total management as a participant in a multidisciplinary team. Obviously, case management by a team may be a new concept to many physicians, and record keeping can be time consuming. Currently, physicians do not receive reimbursement for providing case management services. In view of the expenditure of time and energy, physicians may be reluctant to be responsible for the continuity of care to patients in their homes.

From the patient's viewpoint, surveys reveal that home care is definitely preferred to a nursing home. Furthermore, home care provides the most satisfaction and is the first choice whenever possible.¹⁹ Home care "has always seemed the most efficient, effective, and least traumatic form of medical care."⁸ Nevertheless, Borders²⁰ identified home-care advantages and disadvantages for the patient, the physician, and society. Fear of increased malpractice suits was one disadvantage raised by physicians. However, there does not appear to be any evidence to support that supposition.

Money, or rather the lack of money, provided the stimulus for doing right for the wrong reason. It is estimated that \$817 billion were spent for health care in 1992.¹⁴ An economic and management backlash to the Federal PPS/DRG scheme resulted in "quicker and sicker" entering hospital administration terminology. Hospital administrators endeavored to keep expenses in check and avoid incurring losses. As patients approached the maximum dollar reimbursement established for each of the almost 500 DRGs, that profit/loss situation became acute. Critics charged that patients covered by Medicare were being discharged "quicker" to avoid exceeding the average length of stay, and "sicker" necessitating increased aftercare at home.^{3,21}

In response to the so-called "quicker and sicker" syndrome, the number of Medicare certified home health agencies (HHAs) doubled from about 3,000 to about 6,000 between 1983 and 1985. For the next five years, HHAs grew at a rate of about 20% per year. Today, there are more than 11,000 HHAs: 5,800 Medicare certified HHAs; 300-350 accredited by the Community Health Accreditation Program of the National League for Nursing; and about 2,500 accredited by the Joint Commission on the Accreditation of Healthcare Organizations. That still leaves many home-care providers uncertified and/or unaccredited.

Recently, Medicare initiated a resources based relative value scale for reimbursing physicians for their services to the elderly. Physician visits for a new patient are reimbursed \$48.98 for a low severity problem, \$62.00 for moderate severity, and \$80.29 for a high severity visit. For established patients, the payment schedule is \$37.82, \$49.91, and \$62.62, respectively.²² In addition, experimentation continues with cost containment measures such as resource utilization groups for long-term care, relative intensity measures for nursing services, and ambulatory patient groups for outpatient care.³

As a result of economic considerations overwhelming all other factors, home health care has been promoted as a top-priority cost-containment alternative.

IS HOME CARE THE ALTERNATIVE?

United States Senator Bill Bradley^{23(pvii)} explained the dilemma relative to national health-care policies:

The current health care delivery system views institutional care as the norm and home based care as a promising alternative care system. We need to turn this around. . . Home care should be the norm and institutional care should be the alternative only when home care is not feasible.

Need assessment statistics proclaim that individuals at all ages require home care. Health-care administrators caught up in the cost-containment mentality are adapting innovative marketing and management methods and techniques to "sell" home care as an appropriate alternative.²⁴

Insurance coverage, both governmental and private, severely limits reimbursement for home-care services. Quality assurance and patient classification mechanisms leave much to be desired. Most professional educational institutions and associations have yet to integrate home-care training into their undergraduate, postgraduate, or continuing education curriculums. Structure/process/outcome evaluations and research on home-care costs still need definitive studies.

In a 1992, Universal Health Plan proposed by the Medical Society of the State of New York, Aswad and Menghini¹⁴ urged coverage of long-term care and commented that most state mandates include home health care. Conclusions of the US Bipartisan Commission on Comprehensive Health Care (The Pepper Commission) contained recommendations relative to health system access and to long-term care. Landmark proposals dealt with the specifics of home-care eligibility, benefits, management, and financing. Senator Jay Rockefeller,²⁵ commission chairman, said: "At the heart of the recommendations is a new emphasis on home care. . . And home care in particular would have a respected new place in the American constellation of care."

Commenting that "home health care promises to play an increasingly central role in the future provision of health care," the AMA Councils on Scientific Affairs²⁶ and on Medical Education recommended that training in the principles and practice of home health care be incorporated into the undergraduate, graduate, and continuing education of physicians. In addition, they recommended that home-health care be taught as part of the continuity of patient care; that home-health care assessment be included in hospital discharge planning; that the AMA develop programs to increase physician awareness of the skill and practice of home health care; that the AMA encourage a leadership role for physicians as active team participants in home health-care issues; that the AMA foster physician participation in all present and future home health-care organizational planning initiatives; and that the AMA recommend appropriate reimbursement for physician services in home-health care. To achieve these objectives, a 1992 AMA booklet²⁷ offers guidelines for the medical management of the home care patient and clearly delineates the role of the physician. It covers a range of topics: basic information about home care; the physician-patient relationship; medical management with emphasis on the interdisciplinary team concept, communication, and evalu-

ation; patient's rights and responsibilities; coordination of care/case management; community-based resources; and a state-by-state list of services and resources for the aged.

Beginning in May 1992, the AMA, in conjunction with four state medical societies in Arizona, Illinois, Maryland, and Texas, sought to create a partnership between the Aging Network and physicians.²⁸ A three-hour educational program uses the case study method to train physicians, who in turn become the trainers. These programs on home-care medical management and frontline issues aim to increase physician awareness of community resources in geriatric medical management.

In addition, the AMA national advisory panel issued reports in 1990⁸ and 1991.²⁶ In December 1991, the AMA House of Delegates adopted a report by the Council on Scientific Affairs, "Physicians and Family Caregivers: A Model for Partnership." That report will be published in the near future (Schwartzberg JG, personal communication, 1992).

All of these AMA activities seek to improve physicians awareness of home care, to explain the lines of communication in case management, and to demonstrate techniques to educate family members about self-help procedures. With organized medicine making rapid strides to establish a comprehensive home-care approach, perhaps the title of this article on home care should be paraphrased—let us do the right thing for the right reason!

REFERENCES

1. Paige L: AMA suggests emphasis on home health care. *Am Med News* 1990; 33:10.
2. Home health care society proposed by American College of Physician executives. *Am Acad Home Care Physicians Newsletter* 1992; 4:5.
3. Spiegel AD, Kavalier F: *Cost containment and DRGs: a guide to prospective payment*. Baltimore, National Health Publishing, 1986.
4. Weller C: Home health care. *NY State J Med*. 1978; 78:1957-1961.
5. Driscoll CE: Is there a doctor in the house? *The Female Patient*. 1991; 16:9-10.
6. Meyer M: Experts urge MDs: don't forfeit role to agencies in burgeoning home care. *Am Med News*. 1989; 32:3.
7. Doctors need larger role in home health. (editorial) *Am Med News* 1990; 33:27.
8. Council on Scientific Affairs: home care in the 1990s. *JAMA* 1990; 263: 1241-1244.
9. Spiegel AD: The economics of high technology home care, in Mehlman MJ, Younger SJ (eds): *Delivering High Technology Home Care*, NY, Springer Publishing Co, 1991, pp 23-66.
10. Rogatz P, Schwartz F, Dennis J: A community-based hospice program. *NY State J Med* 1991; 91:500-502.
11. Koska MT: Fostering physician involvement and leadership in home care. *Hospitals*. 1991; 65:48-49.
12. Home care used by 5.7 percent of households. *Hospitals* 1991; 65:14.
13. Aswad CN, Menghini MV: Medical Society of the State of New York Universal Health Plan: a proposal for improving the US health care system. *NY State J Med*. 1992; 92:45-48.
14. Feller BA: *Americans Needing Home Care*. Washington, DC, Government Printing Office, DHHS Pub No. (PHS) 86-1581, March 1986.
15. Thompson LH: *Home Care Experiences of Families with Chronically Ill Children*. Washington, DC, Government Accounting Office, GAO/HRD 89-73, June 1989.
16. Pear R: Abuse widespread in medical sales for care at home. *NY Times* Sept 29, 1991, p 1.
17. Pierre JS: National guidelines needed in DME trade. *Am Acad Home Care Physicians Newsletter* 1992; 4:7.
18. Lutz S: Recuperating at home preferred. *Modern Healthcare*. 1991; 21: 17.
19. Borders CR: Are you ready for the new homelcare? *Patient Care*. 1985; 19:20-46.
20. Kahn KL, Draper D, Keeler EB, et al: *The Effects of the DRG-based Prospective Payment System on Quality of Care for Hospitalized Medicare Patients*. Santa Monica, CA, The Rand Corporation, 1992.
21. Significant increase in reimbursement by Medicare for physician house calls. *Am Acad Home Care Physicians Newsletter*. 1992; 4:1,3.
22. Spiegel AD: *Home Health Care*. Baltimore, National Health Publications, 1987.
23. Spiegel AD: *Strategic Health Planning. Methods and Techniques Applied to Marketing and Management*. Norwood, NJ, ABLEX Publishing Corp, 1992.
24. Rockefeller IV JD: The Pepper Commission. *Am Acad Home Care Physicians Newsletter* 1990; 2:3-4.
25. AMA Council on Scientific Affairs: Educating physicians in home health care. *JAMA* 1991; 265:769-771.
26. American Medical Association, Dept of Geriatric Health: *Guidelines for the Medical Management of the Home Care Patient*. Chicago, 1992.
27. American Medical Association, Dept of Geriatric Health: Project sponsored by the US Administration on Aging National Eldercare Campaign, 1992.

Bilateral, symmetrical leiomyosarcoma of the lower extremities

DANIEL BERINSTEIN, BS; JUAN GODINEZ, MD; ROBERT KIMMEL, MD; WILLIAM D. MAHONEY, MD

Tissue sarcomas comprise 0.7% of all cancers in the United States, with approximately 5,000 new cases and 2,800 deaths reported each year.¹ Sixty percent of soft tissue sarcomas occur in the extremities, with lower extremity tumors occurring three times more often than upper extremity lesions. Roughly 75% of lower extremity sarcomas originate above the knee.² Leiomyosarcoma (LMS) is a rare malignant neoplasm of smooth muscle that constitutes 7.0% of all soft tissue sarcomas.³ Only 105 cases of LMS of the extremities have been reported, all of which were unilateral.⁴ The following report describes a patient with synchronous, symmetrical, bilateral tumors of the lower extremities.

CASE REPORT

A 68-year-old man presented to New Rochelle Hospital Medical Center with a chief complaint of a six week history of bilateral thigh masses. Six months previously, the patient had undergone abdominoperineal resection for adenocarcinoma of the rectum, stage T-3, N-0, M-0, and after surgery, received a combination of radiotherapy (4,500 Cgy in 25 fractions delivered to the pelvis and perineum over 38 days) and chemotherapy (5-fluorouracil, 150 mg and leucovorin, 50 mg). The patient first noted a firm, non-painful mass in his left thigh which, over a period of six weeks, increased in size and became painful. At that time, he noted a smaller mass of similar consistency in his right thigh. The patient had suffered soft-tissue trauma to his back and bilateral thighs during a motor vehicle accident approximately one year prior to his recognition of the thigh masses. He reported a 50 pack per year history of smoking. Past medical and surgical histories were noncontributory.

Physical examination of the lower extremities revealed a 10-cm × 15 cm firm, slightly tender subcutaneous mass located in the distal left thigh, and a 5-cm diameter, firm, non-tender mass in the distal right thigh. There was no inguinal lymphadenopathy. The pulses of the lower extremities were strongly palpable, and motor and sensory function were intact. An abdominal examination revealed a functioning colostomy in the left

lower quadrant with a well healed vertical midline scar. The remainder of the physical examination was unremarkable. Serum laboratory values, electrocardiogram, and chest radiograph were all within normal limits. The carcinoembryonic antigen and CA19-9 tumor antigen markers were both negative.

Magnetic resonance imaging (MRI) studies showed a large 14 cm × 6 cm subcutaneous mass contiguous with the vastus lateralis musculature of the left thigh (Fig 1). The mass was isointense with subcutaneous tissue on T₁, but hyperintense on proton density and T₂ sequences. A smaller 5-cm diameter mass with identical signal intensities was demonstrated in the right thigh (Fig 2). The margins of both masses were noted to be smooth.

The patient underwent bilateral excisional biopsies. Gross pathological inspection of the tumors revealed ovoid, non-compressible masses made up of fleshy tan tissue with a central zone of necrosis. Histologically, the presence of mitotic figures and pleomorphic nuclei (Fig 3) suggested a malignant soft tissue sarcoma. Immunohistochemical stain for smooth muscle actin confirmed LMS, with identical histologic features in both lesions. Electron microscopy showed cellular structures of smooth muscle origin, hence verifying LMS.

On subsequent surgery, the patient underwent bilateral wide local excision of the majority of the skin (including 3-cm margins around the prior biopsy incision), and the majority of the subcutaneous tissue, and the underlying quadriceps muscle group. Frozen section evaluation yielded residual high grade LMS of the left thigh and no evidence of residual right thigh tumor with final specimen margins bilaterally tumor free. The patient regained full unassisted ambulatory capacity and was dis-

charged from the hospital on postoperative day 15. Adjuvant therapy will include 6,000–6,600 CGy of external beam radiation.

DISCUSSION

Park et al⁵ found 66 cases of LMS reported in the literature and added 13 cases. Nine of the 13 lesions had arisen in the lower extremities and many had local or systemic recurrences. Two cases had a second neoplasia, one with craniopharyngioma and the other with colon cancer. Neugut and Sordillo⁴ reported 17 cases of LMS of which 14 presented in the lower extremities. Two cases involving the upper extremities occurred in women with prior mastectomies on the same side. One patient noted a mass seven years following surgery and 4,000 rads of radiation therapy to the chest wall, while the other noted a mass one year following surgery. She did not receive adjuvant radiotherapy.

The initial differential diagnosis of the masses reported in the patient presented here included metastatic rectal carcinoma and soft tissue tumors occurring as spontaneous malignancies after radiotherapy. However, the sites, synchronicity and bilaterality made metastatic rectal carcinoma an unlikely diagnosis, and the lesions were not within the portal of administration of external beam radiation. In addition, the time interval between radiation administration and development of these tumors was minimal. Kim et al,⁶ described a 12-year latent period from irradiation to the development of a soft-tissue sarcoma. Furthermore, Robinson et al.⁷ showed that postirradiation sarcomas generally arise in areas in which surgery could not be performed, which was not the case in this patient.

The literature reports a history of trauma as a possible etiology of soft tissue sarco-

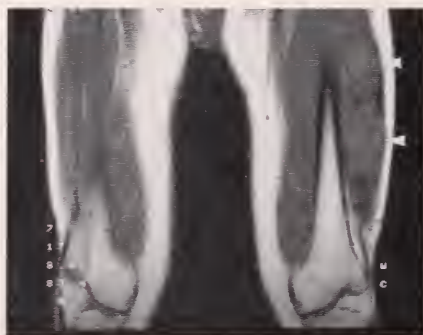


FIGURE 1. MRI T₁-weighted image: Coronal section of lower extremities demonstrating a soft tissue mass in the left thigh (arrows).

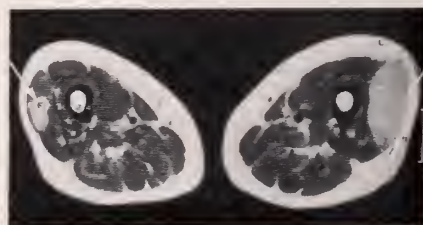


FIGURE 2. MRI T₂-weighted image: Transverse section of lower extremities showing soft tissue masses of bilateral thighs (arrows).

From the Department of Surgery, New Rochelle Hospital Medical Center, New Rochelle, NY.

Address correspondence to Dr Mahoney, Department of Surgery, New Rochelle Hospital Medical Center, 16 Guion Place, New Rochelle, NY 10802.

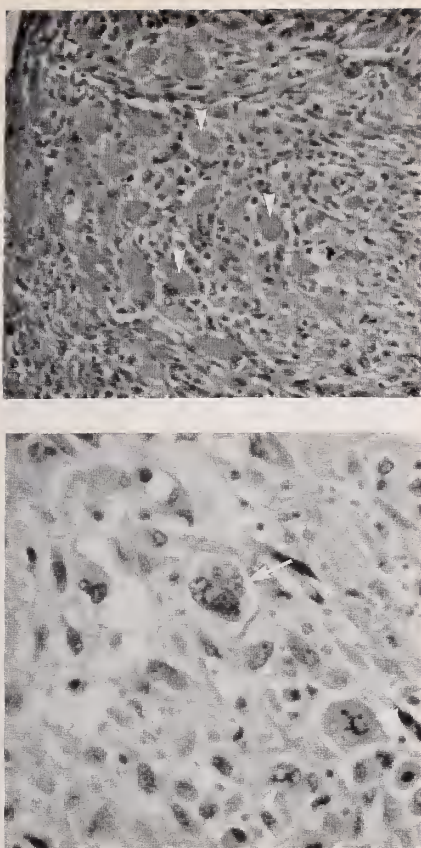


FIGURE 3. Hematoxylin and eosin stain. (Top) Histologic pattern of LMS surrounding normal striated muscle (arrows) (original magnification $\times 180$). (Bottom) Higher magnification demonstrating pleomorphic nuclei (arrow) and mitotic figures (arrow heads; original magnification $\times 500$).

mas.² However, no conclusive relationships have been determined and the trauma experienced may be a direct result of the underlying lesion. The authors believe these lesions originated from the same tumor arising from two distinct sites. Identical histopathological findings confirmed by immunohistochemical and electron microscopic studies support this position.

Soft tissue sarcomas are a diagnostic challenge. Presant et al⁸ showed that for grade I tumors diagnostic concordance between independent pathologists was 83%, grade II, 77%, and grade III, 72%. Tumor grade is the single most important factor in the staging of soft tissue sarcomas. Potter

et al⁹ found tumor size of greater importance to be than tumor site, histologic type, or microscopic margins. However, Donohue et al¹⁰ reported a 14% incidence of distant metastasis in patients with a low grade soft tissue sarcoma; in a third of these cases there were also local recurrences that were unrelated to size or location of the tumor, or adequacy of the surgical margins. In one third of the patients with metastatic disease, metastases were of high grade on histology, analysis suggesting heterogeneity of the primary cancer. The diagnosis of high grade LMS in the above case was based upon the presence of a significant number (greater than five) of mitotic figures per ten high power field.

For diagnostic imaging, Demas et al¹¹ compared computed tomography and MRI and found no differences in accuracy of measurements, detection of tumor depth, or spatial relationship. However, MRI was more accurate in evaluating anatomical compartment and individual muscle involvement, which is important for decisive surgical planning. Differential imaging was judged to be a particularly valuable property of MRI in the determination of histologic origin of the masses presented here.

The management of soft tissue sarcomas of the extremities remains a controversial issue. Surgery excision with adjuvant radiotherapy remains the single most effective treatment modality. Adjuvant chemotherapy has been employed for the treatment of metastasis and local recurrence of high grade soft tissue sarcomas. Trials have shown an initial improvement in disease-free survival, but the overall survival was not significantly improved as compared to control groups.¹² Due to the absence of systemic metastases in the present case, adjuvant chemotherapy was not employed.

The prevailing trend has been to preserve the limbs in the treatment of local disease. Although limb preservation is a laudable goal, the functional outcome of this conservative treatment has not been clearly evaluated. Lampert et al¹³ described limb function by assessing the range of motion, muscle strength, edema, pain, functional capacity, and vocational changes in order to identify those anatomical sites associated with increased risk of developing a poor functional outcome. Patients with soft tissue sarcomas of the lower

extremities are at a higher risk for functional disabilities after wide local excision and radiotherapy. We were therefore particularly attentive to re-establishing post-operative ambulatory function by aggressive physical therapy.

In conclusion, what is clearly needed are randomized, prospective, histologically-specific, multi-institutional protocols to develop the optimal management strategies for these tumors. Despite these deficiencies, the approach to soft tissue sarcomas has undergone a considerable transformation over the last two decades. The evaluation of histologic grading, the functional response to specific treatment protocols, and the systemic treatment with adjuvant chemotherapy will all play a decisive role in the future management of sarcomas.

REFERENCES

- 1986 Cancer facts and figures. *American Cancer Society*, 1986.
- Chang AE, Rosenberg SA, Glatstein EJ, et al: Sarcomas of soft tissues, in DeVita VT Jr, Hellman S, Rosenberg SA (eds): *Cancer: Principles and Practice of Oncology*. Philadelphia, JB Lippincott Co, 1989, pp 1345-1398.
- Enzinger FM, Weiss SW: *Soft Tissue Tumors*. Saint Louis, CV Mosby Co, 1988, pp 402-421.
- Neugut AI, Sordillo PP: Leiomyosarcoma of the extremities. *J Surg Oncol* 1989; 40:65-67.
- Park JJ, Park HC, Choi SH: Leiomyosarcomas of the extremities: angiography as a diagnostic aid. *J Surg Oncol* 1978; 10:407-411.
- Kim JH, Chu FC, Woodard HQ, et al: Radiation-induced soft tissue and bone sarcoma. *Radiology* 1978; 129:501-508.
- Robinson E, Neugut AI, Wylie P: Clinical aspects of postirradiation sarcomas. *J Natl Cancer Inst* 1988; 80:233-240.
- Presant CA, Russell WO, Alexander RW, et al: Soft tissue and bone sarcoma: Histopathology peer review—The frequency of disagreement in diagnosis and the need for second pathology opinions. The Southeastern Cancer Study Group Experience. *J Clin Oncol* 1986; 4:1658-1661.
- Potter DA, Kinsella T, Glatstein E, et al: High grade tissue sarcomas of the extremities. *Cancer* 1986; 58:190-205.
- Donohue JH, Collin C, Friedrich C, et al: Low-grade soft tissue sarcomas of the extremities: analysis of risk factors for metastasis. *Cancer* 1988; 62:184-193.
- Demas BE, Heelan RT, Lane J, et al: Soft tissue sarcomas of the extremities: comparison of MFI and CT in determining the extent of disease. *AJR* 1988; 150:615-620.
- Antman KH, Eilber FR, Shiu MH: Soft tissue sarcomas: current trends in diagnosis and management. *Curr Probl Cancer* 1989; 6:340-367.
- Lampert MH, Gerber LH, Glatstein E, et al: Soft tissue sarcoma: functional outcome after wide local excision and radiation therapy. *Arch Phys Med Rehabil* 1984; 65:477-480.

Ganglioglioma of the mastoid region: a case report

MARITESS G. DEJESUS-UICHANCO, MD; TUNG PUI POON, MD; KUN-YOUNG CHUNG, MD;
I. WEITZNER, MD

Gangliogliomas are rare, slow growing neoplasms of the central nervous system (CNS) which are composed of mature neurons and neuroglial elements. They comprise 0.3% to 0.4% of all brain tumors and occur most often in children and young adults.¹ The most common sites are the floor of the third ventricle, hypothalamus, and temporal lobe.² They have rarely been described in the following locations: spinal cord,³⁻⁶ brain stem,^{7,8} fourth ventricle,⁹ cerebellum,^{10,11} basal ganglia,² pineal region,¹² thalamus,¹³ intrasellar region,¹⁴ and optic nerve.¹⁵ Twenty-seven cases of "congenital ganglioglioma," nasal in location, were recorded in the Armed Forces Institute of Pathology (AFIP) Registry in 1964 and were thought to represent congenital herniation of brain tissue.¹⁶ We describe a patient with a ganglioglioma in the mastoid region. To our knowledge, this is the first case reported of the tumor in this location. We review the literature and the immunohistochemical studies of this neoplasm.

CASE REPORT

A 56-year-old woman was admitted with complaints of mental confusion, disorientation, fever, and chills. The patient had a history of atherosclerotic heart disease and myocardial infarction two years previously. Medications prior to the present admission consisted of diltiazem, 60 mg orally three times a day; nadolol, 40 mg orally daily; furosemide, 20 mg orally daily; and nitroglycerin, 5 mg transdermal patch daily.

On admission, the patient was alert and slightly obese. An electrocardiogram showed borderline left ventricular hypertrophy and evidence of an old myocardial infarction. She was treated for an upper respiratory tract infection, with possible pneumonia, and was given erythromycin, 500 mg orally four times a day. A complete blood cell count was unremarkable except for leukocytosis with a shift to the left. Serum chemistry studies showed a glucose level of 233 mg/dL.

On the second hospital day, nausea, vomiting, and severe headache developed. A spinal tap was done which revealed an opening pressure of 230 mm Hg. The protein level was 130 mg/dL; white blood cell count, 5,300/mm³; and red blood cell count, 130/mm³. Meningitis was suspected and she was started on cefotaxime, 2 g intravenously every 12 hours.

In a few days, the fever subsided, at which time the patient complained of a left earache. A computed tomography (CT) scan of the ear revealed left-sided mastoiditis (Fig 1). The patient underwent mastoidectomy nine days after admission. At operation, the entire tegmen was found to be covered by pinkish white tissue which completely occluded the antrum and the superior part of the mastoid. The tegmen was noted to be intact on evacuation of the tissue. The patient's symptoms improved after surgery. She remained afebrile and was discharged 18 days after admission; her complete blood cell count and serum chemistries were within normal limits.

Pathology. The gross specimen consisted of multiple fragments of granular pinkish gray, soft to firm tissue measuring 0.8 × 0.7 × 0.5 cm in aggregate. Microscopic examination showed numerous fibrillary astrocytes mixed with mature neurons (Figs 2, 3). No vascular invasion or mitoses were noted. The immunohistochemical stains for glial fibrillary acidic protein and neuron specific enolase were positive in the astrocytes and neurons, respectively. The pathologic diagnosis was ganglioglioma.

DISCUSSION

To our knowledge, this is the first reported case of ganglioglioma occurring in the mastoid region. Gangliogliomas are rare neoplasms of the CNS and comprise 0.3% to 0.4% of all brain tumors. The term "ganglioglioma" was initially used by Loretz in 1870¹⁷ to describe a tumor in the thoracic cavity. Courville¹⁸ adopted the term in 1930 for tumors of the CNS composed of ganglion cells and neoplastic glial cells. Rubinstein² in 1972 reclassified these neoplasms according to the degree of differentiation and relative preponderance of ganglions or neuroglial elements. The strict

designation of ganglioglioma was given to those tumors that had a predominance of glial cells. Those rarer tumors with a relatively large proportion of neuronal elements were designated as ganglioneuromas.

Gangliogliomas are typically intracerebral in location. In 1964, Ash and associates reported 27 cases of nasal gangliogliomas in the AFIP Registry, which were considered to be congenital herniation of glial tissue or "brain extrusion."¹⁶ The tumor, as they described it, contained true neurons. The current edition of the AFIP fascicle on tumors of the upper respiratory tract and ear provides no discussion of these "congenital gangliogliomas" in temporal bone. Instead, several cases of temporal bone encephaloceles in the middle ear, as well as ectopic CNS tissue composed solely of glial elements are described. The latter are included in the category "tumor-like or questionable neoplastic lesions," suggesting that their exact nature is unsettled.¹⁹

The case we describe appears to be a true ganglioglioma because of the following features: no disruption of bone integrity noted at the time of surgery; absence of a leptomeningeal component in the tumor; absence of postsurgical otorrhea; and definite identification of neurons based on light microscopy and immunohistochemical studies.

Gangliogliomas occur most frequently in children and young adults, usually before 30 years of age. However, the age range may be from 14 to 58 years. These tumors are slow growing and tend to be well circumscribed, with symptoms varying according to their location. For instance, longstanding focal seizures are a common presenting complaint, especially with tumors involving the temporal lobe.^{20,21} Those occurring in the area of the third ventricle and hypothalamus may present as problems of appetite or water imbalance.

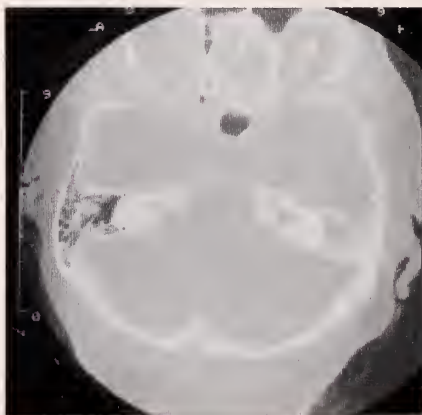


FIGURE 1. Axial view of petrous bone shows an antral soft tissue mass filling the left antral region without definite bone destruction (arrow). These CT scan findings are nonspecific.

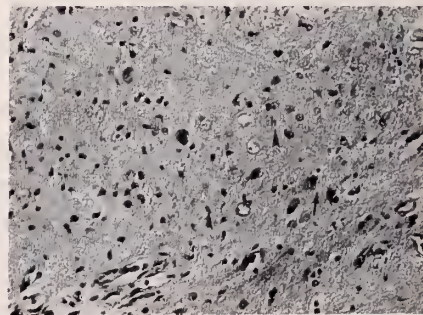


FIGURE 2. Mastoid tumor showing mature neurons (arrow) and fibrillary astrocytes (arrowhead); hematoxylin and eosin stain; original magnification × 100.

From the Departments of Pathology, Mount Vernon Hospital, Mount Vernon, NY (Drs De Jesus-Uichanco and Chung) and New York Medical College-Metropolitan Hospital Center, New York, NY (Dr Poon) and the Department of Radiology, New York Medical College-Lincoln Hospital and Medical Center, Bronx, NY (Dr Weitzner).

Address correspondence to Dr Poon, Department of Pathology, Metropolitan Hospital Center, 1901 First Avenue, New York, NY 10029.

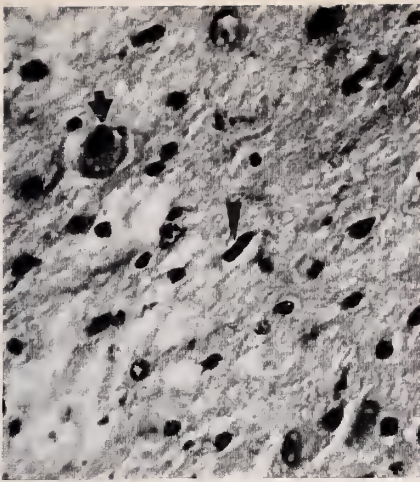


FIGURE 3. Mature neurons (arrow) mixed with fibrillary astrocytes (arrowhead; hematoxylin and eosin stain; original magnification $\times 400$).

On gross examination, the tumors appear solid, small, and firm, and are sharply delineated with a granular pinkish surface. Frequently, foci of calcification and cyst formation are seen and both are detectable on CT scan.

The histologic appearance varies according to the predominant cell type as described above.² Tumors that are true "gangliogliomas" show ganglion cells with large round vesicular nuclei, prominent nucleoli, and abundant cytoplasm. They may assume bizarre shapes with occasional giant cells and may show misaligned cell processes. The glial elements are usually fibrillary astrocytic cells, and in some cases, may be oligodendroglial. They generally exhibit benign cytologic features, and they

are often misdiagnosed as astrocytomas, so that a careful search for abnormal neurons is mandatory.

The prognosis is favorable since tumor growth is insidious. These tumors are generally regarded as benign, although recurrence is a possibility and malignant transformation to glioblastoma may rarely occur.^{2,13,21,22} Once regarded as hamartomas or congenital malformations, gangliogliomas are currently considered to be true neoplasms due to expansile clinical behavior.

Cerebral gangliogliomas are treated with either total or subtotal extirpation. Radiation therapy is indicated only if there is histologic evidence of malignancy. The treatment of choice for mastoid ganglioglioma is complete tumor excision. There is a paucity of clinical data to recommend use of radiotherapy.

REFERENCES

1. Zulch KJ: *Brain Tumors: Their Biology and Pathology*. 2nd ed. Berlin, Springer-Verlag, 1965, pp184.
2. Rubenstein LJ: *Tumors of the Central Nervous System. Atlas of Tumor Pathology*, second series, fascicle 6. Washington, DC, Armed Forces Institute of Pathology, 1972, pp158-167.
3. Albright L, Byrd RP: Ganglioglioma of the entire spinal cord. *Childs Brain* 1980; 6:274-280.
4. Bevilacqua G, Sarnelli R: Ganglioglioma of the spinal cord: a case with a long survival. *Acta Neuropathol* 1979; 48:239-242.
5. Epstein N, Epstein F, Allen JC, et al: Intractable facial pain associated with a ganglioglioma of the cervical medullary junction: report of a case. *Neurosurgery* 1982; 10:612-616.
6. Wald U, Levy PJ, Rappaport ZH, et al: Conus ganglioglioma in a two and one half year-old boy. *J Neurosurg* 1985; 62:142-144.
7. Garcia CA, McGarry PA, Collada M: Ganglioglioma of the brainstem: case report. *J Neurosurg* 1984; 60:431-434.
8. Gondim-Oliveira JA, Choux M: Tumeurs du tronc cerebral chez l'enfant. *Neurobiol* 1982; 45: 167-180.
9. Ponzi S, Corgioli E, Cocchini F, et al: Apporto diagnostico dell'esame otv nella patologia espansiva del IV ventricolo. *Minerva Otorinolaringol* 1981; 31:411-416.
10. Johansson JH, Reke HL, Roessmann U: Gangliogliomas: pathological and clinical correlation. *J Neurosurg* 1981; 54:58-63.
11. Mizuno J, Nishio S, Barrow D, et al: Ganglioglioma of the cerebellum: case report. *Neurosurg* 1987; 21:584-588.
12. Packer RJ, Sutton LN, Rosenstock JG, et al: Pineal region tumors of childhood. *Pediatrics* 1984; 74:97-102.
13. Sutton LN, Packer RJ, Rorke LB, et al: Cerebral gangliogliomas during childhood. *Neurosurg* 1983; 13:124-128.
14. Hasegawa M: Transseptal approach to the sphenoid sinus and the pituitary gland. *Jibi Inkoka* 1982; 54:141-148.
15. Gritzman M, Snyckers FD, Proctor M: Ganglioglioma of the optic nerve: a case report. *S Afr Med J* 1983; 63:863-865.
16. Ash JE, Beck MR, Wilkes JD: *Tumors of the Upper Respiratory Tract and Ear. Atlas of Tumor Pathology*, section IV fascicle 12 and 13. Washington, DC, Armed Forces Institute of Pathology, 1964, pp79-81.
17. Loretz W: Ein fall von ganglioscom neuron (ganglion). *Virchows Arch* 1870; 49:435.
18. Courville CB: Ganglioglioma: tumor of the central nervous system—review of literature and report of two cases. *Arch Neurol Psychiatr* 1930; 24: 439-491.
19. Hyams VJ, Batsakis JG, Michaels L: *Tumors of the Upper Tract and the Ear. Atlas of Tumor Pathology* 2nd series, fascicle 25. Washington, DC, Armed Forces Institute of Pathology, 1988, pp 304-305.
20. Demierre B, Stichnoth FA, Hori A, et al: Intracerebral ganglioglioma. *J Neurosurg* 1986; 65: 177-182.
21. Kalyan-Raman U, Olivero WC: Ganglioglioma: a correlative clinicopathological study of 10 surgically treated cases with follow up. *Neurosurg* 1987; 20:428-433.
22. Russell DS, Rubinstein LJ: Ganglioglioma: a case with long history and malignant evolution. *J Neuropathol Exp Neurol* 1962; 21:185-193.

Acute cor pulmonale due to tumor emboli

Diagnosis by pulmonary artery catheterization

JANET M. SHAPIRO, MD; DAVID E. AVIGAN, MD; MARK K. WARSHOFKY, MD;
ELLEN GREENEBAUM, MD; RANDOLPH P. COLE, MD

The lung is a frequent site of metastatic tumor involvement. Hematogenous dissemination may lead to lymphangitic carcinomatosis, parenchymal nodules or tumor emboli in the pulmonary circulation, with the latter occasionally being associated with the development of cor pulmonale.¹⁻⁴ The diagnosis of pulmonary involvement by malignancy often requires lung biopsy. Re-

cently, cytologic examination of the pulmonary microvasculature has been used in the diagnosis of lymphangitic carcinomatosis and tumor emboli.^{5,6} We report here a patient with acute cor pulmonale due to tumor microemboli diagnosed by pulmonary artery catheterization.

CASE REPORT

A 44-year-old woman with breast cancer presented with shortness of breath. Eighteen months prior to admission, biopsy of a left breast mass revealed invasive intraductal carcinoma. She received three cycles of adriamycin (total 270 mg/m²) with a reduction in tumor size and then underwent a left modi-

fied mastectomy. Two of eight regional lymph nodes contained metastatic carcinoma. Radiation therapy (total 5,000 Gy) was administered to the left chest wall. Cyclophosphamide (600 mg/m²), methotrexate (40 mg/m²), and 5-fluorouracil (600 mg/m²) were then administered intravenously every 21 days for the next six months. The patient was then maintained on tamoxifen (20 mg/day) and did well until one month prior to admission when she developed shortness of breath with exertion. A chest radiograph revealed a large right pleural effusion and thoracentesis was performed. Clusters of malignant cells diagnostic of adenocarcinoma were present on cytologic examination (Fig 1a). Four days prior to admission, she received intravenous cyclophos-

From the Departments of Medicine and Pathology, College of Physicians and Surgeons, Columbia University, New York, NY 10032.

Address correspondence to Dr Shapiro, Pulmonary Division, Department of Medicine, St Luke's-Roosevelt Hospital Center, 114th Street and Amsterdam Avenue, New York, NY 10025.

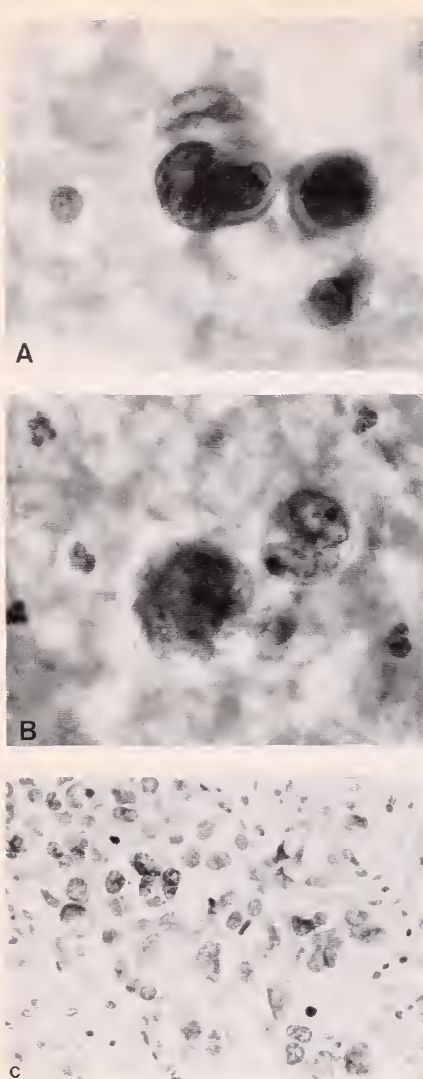


FIGURE 1. Adenocarcinoma in pleural fluid (a) and in blood sample from wedged pulmonary catheter (b). Note the large cell size, high nuclear-cytoplasmic ratio, nuclear hyperchromasia, and, in (b), the nucleolar prominence (original magnification $\times 250$; Papanicolaou stain). Invasive ductal carcinoma of the left breast (c). Note the morphologic similarity of the malignant cells to those seen in Figs 1a and b (original magnification $\times 160$; hematoxylin and eosin stain).

phamide (900 mg) and 5-fluorouracil (600 mg) and was started on prednisone, 40 mg daily.

The patient subsequently presented to the hospital with progressive dyspnea and orthopnea. On arrival in the emergency room she was in marked respiratory distress with a respiratory rate of 40/min, a systolic blood pressure of 70 mm Hg, heart rate of 110/min and temperature of 38.3°C. Examination was notable for jugular venous distention, an S_3 gallop at the left sternal border and an increased pulmonic closure sound. Lung examination was remarkable for dullness and diminished breath sounds over the lower two thirds of the right hemithorax and a clear left lung field. There was no hepatosplenomegaly or edema. The patient was treated with intrave-

nous normal saline and norepinephrine and admitted to the Medical Intensive Care Unit. Laboratory data revealed a packed red cell volume of 31%, and a white blood cell count of 18,000/ μ L. Arterial blood gas studies while receiving 100% O_2 via a non-rebreathing face mask revealed pH 7.31, PCO_2 , 17 mm Hg, and PO_2 , 87 mm Hg. A chest radiograph showed an enlarged heart, large central pulmonary arteries and a large right pleural effusion. The remainder of the lung fields were clear. An electrocardiogram revealed sinus tachycardia with a QRS axis of 45°. A thoracentesis was performed and one liter of serosanguinous pleural fluid was removed; it had a protein concentration of 4.8 g/L, glucose concentration of 173 mg/dL, and lactate dehydrogenase concentration of 401 U/L. Subsequent cultures of blood and pleural fluid were negative for bacterial and fungal growth. An echocardiogram showed marked dilatation of the right atrium and right ventricle, normal left ventricular function and no pericardial effusion. A lower extremity ultrasound study was negative for deep vein thrombosis.

The patient received intravenous fluids and pressors to maintain a systolic blood pressure of 100 mm Hg. Pulmonary artery catheterization revealed a right atrial pressure of 15 mm Hg, a right ventricular pressure of 40/15 mm Hg, a pulmonary artery pressure of 40/30 mm Hg, and a pulmonary capillary wedge pressure of 20 mm Hg. The cardiac output by thermodilution technique was 3.4 L/min. The clinical impression was massive pulmonary thromboembolism versus tumor embolism. Intravenous heparin (800 U/hr) and cefuroxime (750 mg every 8 hours) were started. On the second hospital day, a ventilation-perfusion scan revealed a matched defect at the right base. Subsequent pulmonary angiography showed a pulmonary artery pressure of 58/26 mm Hg and no evidence of embolism. Anticoagulation was discontinued and a chest tube placed with removal of two liters of fluid. With the pulmonary artery catheter in the balloon-occluding position, a 10 mL sample of blood was withdrawn and submitted for cytological examination. After centrifugation of the blood sample, an aliquot of the buffy coat was spread on two slides and stained according to the method of Papanicolaou. Rare small clusters of adenocarcinoma cells (Fig 1b) morphologically similar to those seen in the previously examined pleural fluid (Fig 1a) and also to the initial invasive ductal carcinoma (Fig 1c) were identified.

The patient's respiratory status improved and pressors were discontinued on the third hospital day. She underwent tetracycline pleurodesis and on the 15th day began a course of chemotherapy with cyclophosphamide, mitoxantrone, 5-fluorouracil and dexamethasone. On the 18th hospital day, the patient complained of difficulty breathing and suffered a witnessed respiratory arrest. In spite of resuscitation efforts, the patient expired. Permission for autopsy was denied.

DISCUSSION

The incidence of microscopic tumor emboli to the lung is not known. One autopsy series found an incidence of 2.4% among

cancer patients.⁷ Over 30 cases of tumor embolization leading to pulmonary hypertension and cor pulmonale have been reported.¹⁻⁴ Typically, these patients presented with dyspnea and hypoxemia and often clear chest radiographs. Pathological examination revealed malignant cells filling the small pulmonary arteries and arterioles. The diagnosis of pulmonary involvement with tumor is usually made by lung biopsy or at autopsy. Pulmonary microvascular cytology has been reported to be diagnostic in ten patients, eight with lymphangitic carcinomatosis and two with likely tumor embolism.^{5,6} In the latter two cases, the leading differential diagnosis in a patient with prostate cancer and a patient with breast cancer was thromboembolism versus tumor embolism. Chest radiographs in both situations showed clear lung fields. The final diagnosis of tumor embolism was confirmed by transbronchial biopsy in the patient with prostate carcinoma. In the second case, a low probability ventilation-perfusion scan made tumor embolism the more likely clinical circumstance.⁶

The patient presented here had dyspnea and was in right heart failure. Pulmonary artery catheterization documented pulmonary hypertension. The finding of malignant cells in the pulmonary microvasculature indicated lymphangitic carcinomatosis or tumor embolism. In this case, the absence of typical chest radiographic findings of lymphangitic carcinomatosis and the rapidly developing cor pulmonale would be most consistent with microscopic tumor embolization. It is possible that massive tumor embolization to an already compromised pulmonary vascular bed was responsible for her respiratory arrest. When a patient with carcinoma presents with dyspnea, hypoxemia and evidence of right heart failure, the differential diagnosis usually includes massive thromboembolism, tumor embolism and pericardial tamponade. Placement of a pulmonary artery catheter may be helpful in allowing hemodynamic assessment and cytological examination of the pulmonary microvasculature.

REFERENCES

1. Marin JJ, Bilnoski W, Huseby JS: Acute cor pulmonale resulting from tumor microembolism. *West J Med* 1980; 132:77-80.
2. Margolis MD, Jarrell BE: Pulmonary tumor microembolism. *South Med J* 1985; 78:757-758.
3. He X, Tang Y, Luo Z, et al: Subacute cor pulmonale due to tumor embolization of the lungs. *Angiology* 1989; 40:11-17.
4. Case Reports of the Massachusetts General Hospital: Case 30-1987: *N Engl J Med* 1987; 317:225-235.
5. Masson RG, Krikorian J, Lukl P, et al: Pulmonary microvascular cytology in the diagnosis of lymphangitic carcinomatosis. *N Engl J Med* 1989; 321:71-76.
6. Masson RG, Ruggieri J: Pulmonary microvascular cytology, a new diagnostic application of the pulmonary artery catheter. *Chest* 1985; 88:908-914.
7. Kane RD, Hawkins HK, Miller JA, et al: Microscopic pulmonary tumor emboli associated with dyspnea. *Cancer* 1975; 36:1473-1482.

Address correspondence to Editor, New York State Journal of Medicine, 420 Lakeville Road, Lake Success, NY 11042. Letters should be typed double-spaced and include the signature, academic degree, professional affiliation, and address of each author. Preference is given to letters not exceeding 450 words, and every effort will be made to assure prompt publication after editorial review. All letters are personally acknowledged by the Editor.

The Journal as an excellent and thorough resource

TO THE EDITOR: At the November 24, 1992, Council of the Medical Staff meeting of Strong Memorial Hospital the topic of "Advance Directives and How They are Being Addressed in our Hospital" was discussed. The article by Joseph J. Fins, MD, "The patient self-determination act and patient-physician collaboration" in New York State from the November 1992 issue of the *New York State Journal of Medicine* was used by the council members as an excellent and thorough resource in this discussion.¹ The *New York State Journal of Medicine* has consistently provided special articles of this type which are not readily found in other medical publications. On behalf of the Council of the Medical Staff of Strong and myself please accept our sincere thanks.

CARL ANDRUS, MD
Chairman, Council of the Medical Staff
Strong Memorial Hospital
601 Elmwood Avenue
Rochester, NY 14642

1. Fins J: The patient self-determination act and patient-physician collaboration in New York State. *NY State J Med* 1992; 92:489-493.

Keep socio-medical economic inserts out of the Journal

TO THE EDITOR: I read with great interest the article by Dr Milton Gordon, Chairman of the Committee on Publications, Library, and Archives on "The status of the *New York State Journal of Medicine*: Where are we?"¹ I must, however, disagree with his recommendation for placing in the *Journal* an "insert of several pages, prepared by the Division of Communications, covering in-depth important society news and activities, as well as socio-economic issues."

This seems to me rather like introducing a foreign body into what Dr Gordon himself called "a medical journal of excellence . . . ranked among the top five percent of peer-reviewed medical journals." Inserts so different in content from the material in the *Journal* do not belong there, but in *News of New York*. I do not feel that including inserts in the *Journal* would "ensure high readership levels." Like most readers of medical journals, if I set aside time for serious reading I do not want to be distracted by irrelevant material.

I therefore ask that Dr Gordon and the members of the Committee on Publications, Library, and Archives rescind the recommendation for inserts. For me, inserts are like transplants—vulnerable to rejection by a discriminating readership that I believe wants

its medical journals unadulterated. In a word, if it ain't broke, don't fix it.

FRED B. CHARATAN, MD
11 Jayme Drive
North Babylon, NY 11703

1. Gordon M: The status of the *New York State Journal of Medicine*: Where are we? *NY State J Med* 1993; 93:7-11.

High standards for the New York State Journal of Medicine

TO THE EDITOR: I have always enjoyed reading the *New York State Journal of Medicine*. I think it is one of the outstanding state medical journals that I have had the opportunity to read. I congratulate you on your high standards, and I wish you continued success.

HARVINDER S. LUTHRA, MD
Division of Rheumatology
Department of Internal Medicine
Mayo Clinic
Rochester, MN 55905

Support for the Journal

TO THE EDITOR: I am writing to express my appreciation for the thorough, lucid, and persuasive article which Dr Milton Gordon wrote for the January 1993 issue of the *Journal*.¹ I think it would be a disservice to the Society to change the mission and content of the *Journal*. The high regard which the *Journal* enjoys reflects positively on the Society and its members. To change it to a purely socio-economic tabloid would tend to confirm the mistaken notion that physicians are only interested in the economic aspects of medicine.

I read the *Journal* practically cover-to-cover and find it informative and interesting as do many others to whom I have spoken. Keep up the good fight to preserve the *Journal* as a peer-reviewed clinical and scientific publication.

ALBERT M. SCHWARTZ, MD
Past Treasurer
Medical Society of the State of New York
410 East 57th Street
New York, NY 10022

1. Gordon M: The status of the *New York State Journal of Medicine*: Where are we? *NY State J Med* 1993; 93:7-11.

The New York State Journal of Medicine as the principal benefit of Medical Society membership

TO THE EDITOR: I received the January issue of the *New York State Journal of Medicine*

and was shocked to find that there is consideration being given to transforming the *Journal* into a throw-away tabloid. It is unthinkable that the *Journal* be discontinued as a peer-reviewed scientific publication. Who would even conceive of such a thing?

I love the *Journal*. It is our *Journal*, and it is extremely good. I look forward to it and to seeing the names of colleagues and friends as contributors from time to time. I will say this. If the Society stops publishing the *Journal* as a peer-reviewed scientific publication, it will no longer receive my dues. Reading the *Journal* is the only pleasure that I get for my Society dues.

ANTHONY DiBENEDETTO, MD
11 Horse Hill Rd
Brookville, Glen Head, NY 11545

Support for the New York State Journal of Medicine

TO THE EDITOR: When I read Dr Milton Gordon's article on the status of the *Journal*,¹ I became saddened and angered. The Medical Society of the State of New York produces one of the best state medical journals, a journal of national acclaim. Dr Gordon skillfully lists all the reasons to maintain such a journal. That the *Journal* produces a profit is merely icing on the cake.

Medicine is not yet so "advanced" that we can afford to discard journals, books, and libraries to be replaced by computers, gadgets, and throw aways. Personally, I look forward each month to the *Journal* with the mix of pertinent and timely scientific articles, history, philosophy, or art which always appeal to my narrow pre-medical academic yearnings for culture. I also look forward to the commentaries, which are always scholarly discussions, sometimes of the sort of items included in a socio-economic tabloid.

Furthermore, I wholeheartedly agree that a 28.24% return rate on the Member Needs Survey negates any conclusions except that 71.76% of those surveyed did not return their questionnaires. Usually, by the way, those in agreement with present conditions do not return, while those seeking change do return. Dr Gordon's list of experts is impressive, but omitted any or all the statistics departments of the medical colleges in New York State, which does surprise me.

I wish to thank the staff of the *Journal* and Dr Gordon and his committee for their efforts to produce a journal of this degree of excellence. I also fear that the powers wishing to downgrade the *Journal* to a tabloid may also seek to replace Dr Gordon and the dedicated members of the Committee of Publications, Library, and Archives. I hope this does not happen. I hope to see the

Journal remain as a peer-reviewed, clinical and scientific journal and improve.

I could sign with a list of titles, but I wish to speak out as just an ordinary member of the Medical Society, who probably forgot to return his survey.

GERALD ENTE, MD
530 Old Country Road
Westbury, NY 11590

1. Gordon M: The status of the *New York State Journal of Medicine*: where are we? *NY State J Med* 1993; 93:7-11.

Support for continuing the *New York State Journal of Medicine* as a peer-reviewed scientific publication

TO THE EDITOR: I would like to add my voice to the many others who have expressed their strong feelings that the *New York State Journal of Medicine* be continued as a peer-reviewed scientific publication.

I have been a member of the Society for over 35 years and have found the *Journal* to be a high-quality publication. I trust you will see to it that my opinion as well as those of countless others, who I am sure have communicated with you, are brought to the attention of the Council and the House of Delegates.

I sincerely believe that discontinuation of the *Journal* as a peer-reviewed publication would constitute a serious tragedy.

LEONARD FOX, MD
65 Shrubhollow Rd
Roslyn, NY 11576

Thanks from the Committee on Publications, Library, and Archives for support of the *New York State Journal of Medicine*

TO THE EDITOR: On behalf of the Committee on Publications, Library, and Archives I want to thank Drs Andrus, Charatan, Luthra, Schwartz, DiBenedetto, Ente, and Fox for their positive comments about the *Journal*. We fully agree with Dr Ente, as do many who have contacted us, that the most striking result of the Member Needs Survey is that 71.76% of those surveyed did not respond. The biostatisticians and epidemiologists we consulted characterized the low 28.24% response ratio to this survey as "biased" and its results as totally "unreliable." Yet, the Task Force on Publications and Communications framed its assessment of the *Journal* within the context of the invalid results of this survey.

In planning a new readership survey, we did not seek advice about valid response rates from biostatisticians and epidemiologists in New York State medical schools since many of them peer-review articles for the *Journal* and strongly support it. Their opinions on this issue and the invalid Member Needs Survey results thus could have been characterized as biased by those who want to eliminate the *Journal* as we know it. Therefore, we solicited

advice from experts who were not closely associated with the *Journal*.

In response to Dr Charatan, our proposal for a socio-medical economic insert was intended to respond to the Society's current fiscal capabilities while keeping such a publication distinct from the *Journal*.

Once again, I want to assure society members and other readers that the Committee on Publications, Library, and Archives is doing its best to support the continuance of the *Journal* as a peer-reviewed clinical and scientific journal. The Committee is also doing its best to counter the misinformation being disseminated by those who wish to transform the *Journal* into a throw-away socio-medical economic tabloid.

MILTON GORDON, MD
Chairman,
and the Members of the Committee on
Publications, Library, and Archives
Medical Society of the State of New York
420 Lakeville Road
Lake Success, NY 11042

Remember when

TO THE EDITOR: Remember when medicine used to be fun? When we grumbled because it was the style to do so? When despite our crabbing we still had the feeling that medicine was great and that it would be wonderful if our children followed in our footsteps? So what happened?

I feel that we've become a tribe of grouchers, grumblers, and grippers. We grumble when a patient calls us at odd hours. We gripe when they call us too early and we complain when they've waited too long and are really ill. We've somehow gotten the feeling that patients get sick just to annoy us—deliberately.

We resent being asked to make house calls and we resent having too many sick people in the office spreading germs. We complain that we are working too hard and too long, that the competition is getting stronger. We grouse when so-and-so stole one of my patients.

We object to working so hard for so little, and that the government is taking most of what we make. We are constantly seeking new ways to increase our activity; to increase our earning capacity. We employ public relations firms of one sort or another to advertise our abilities. We use advertisements, radio and TV, all of which were condemned in the "good old days." We recognized that our practices were built on someone else's patients and we accepted it. We tried a little harder not to lose too many patients.

If we are not happy and content doing the thing we do best and should like the most, how can we manifest an enthusiasm we do not feel? How can medical and premedical students be influenced in a positive fashion, if those whom we would have them emulate present medicine in a negative way? How can a teacher create an allegiance to a family when the families most often are vague names and faces intruding on his limited time? How can he feel a personal intimacy when some of the complaints he hears are completely foreign to his frames of reference? They only serve to remind him of his inadequacy after

he has so carefully built an image of his omnipotence.

Do you remember when the chiefs of staffs made grand rounds? What excitement! What tension! Do you recall the murmurs and the jostling to get a good spot—to see and hear "The Great Clinician" (and what hospital did not have one)? What a great feeling it was to be praised. Even being embarrassingly wrong was a great experience. Now we are too busy. We must divide our attention and our time. Too many hospitals, too many meetings and too much paperwork have carved us into too many pieces.

Do you remember the dignity and the pride with which doctors greeted nurses and how the nurse rose to her feet? This was not the mark of servility, but a token of respect—one for the other. How we made rounds with the nurses assisting and taking notes? Ego building? Certainly, but it added to the witchdoctor-like aura that made the patient know he would get better.

Unfortunately, the doctor has become a provider, a vendor, or a supplier. He has been lowered to the level of a tradesman. I do not mean to denigrate any honest occupation, but the air of confidence that often accounted for success in medicine cannot exist in an atmosphere void of differences in ability and knowledge.

I defer to my plumber and my electrician. Certainly, I deserve the same respect. In place of this atmosphere, I have been told to take the patient into my confidence and make a partner of him. Yes, I will take him into my confidence, and I will try to educate him so that he may be better able to cooperate. However, if I want a partner, I'll open a candy store or a laundry. What I want is someone to listen to me, and to follow my instructions. We've educated patients to a point where their knowledge interferes with good medical practice; to a point where they follow the newspapers, the magazines and their friends, and then tell us how they want us to treat them.

So what have I said? Nothing of great import, but I think it is time for the doctor to review his past and plan for his position in the future of medicine. Let's rescue medicine from the hands of the legal body and from the hands of the political body so that we can get back to practicing medicine as we know it can and should be done. Perhaps, we would be more militant. Sometimes it appears that this attitude works when all else fails.

Until we all learn to accept our respective places in the field of Medicine, pay more attention to the overall picture and are ready to fight for what we know is best, we will be unhappy. I don't like being unhappy because I remember when it was fun to be a doctor.

EDWIN MATLIN, MD
220 Stewart Avenue
Garden City, NY 11530

Physicians in distress

TO THE EDITOR: The character of American health care is under fire. Urged by a precipitous rise in the number of malpractice suits, and the resultant insurance crisis, a

wider range of authorities have begun to police medical conduct. Once supervised by state boards and peer review, physicians are now forced to contend with broader, more invasive, and more vigilant types of regulatory bodies. Physicians in Distress (PID), a moniker coined by the corps of advisors who service the medical community's interactions with governing agencies, is increasingly used to identify the escalating numbers of professionals assailed for the quality of treatments which they provide.

The passage of The Health Care Quality Improvement Act of 1986, Title IV of Public Law 99-660, is an example of a dramatic new development. This legislation prompted the establishment of the National Practitioner Data Bank, an agency charged solely with the task of collecting and dispensing physicians' records of censure. Operated by Unisys Corporation, the data bank is sponsored by the US Department of Health and Human Services.

The network's objectives are to inhibit the state-to-state movement of incompetent medical professionals, and encourage peer review in the disciplinary proceedings of delinquent practitioners. These tasks are to be facilitated by measurements outlined in the statute. Title IV places strict reporting requirements on all physicians and dentists, as well as malpractice insurers, licensing boards, hospitals, and professional societies. The Data Bank can release any probationary action, malpractice payment, review proceeding, or professional conduct inquiry as public information. However, peer review actions are protected by Section 402 of Public Law 100-177, which also provides civil suit immunity for those who identify unqualified practitioners, or furnish expert testimony for the prosecution.¹ Hospitals, licensing boards, professional societies and plaintiff's attorneys may request data in all 50 states. Physicians are also entitled to place inquiries relative to their own files. Malpractice insurers are an exception in that they are prohibited from examining the information which they must otherwise disclose.

Considering the interest in protecting the public from incapable or negligent practitioners, the data bank is ideal. Providers of inadequate care should find themselves restricted. On the other hand, it is alarming to recognize that the government did not demand a clearinghouse of criminal records, but instead chose to target health care professionals. This is an unnerving comment on the relationship between the bureaucracy and the medical community.

The full influence of "Big Brother" has yet to be realized. Having become operable in September 1990, many doctors are still unsure of the role that the data bank will play in their careers. The issue of greatest concern to competent physicians is the potential for this system to cause widespread professional damage should their activities be reviewed or curbed. Due to the fact that this reprimand can become public, a "ripple effect" could result in other organizations concluding that the measure was substantial enough to warrant imposing additional restrictions. This could lead to the revocation of state licenses,

narcotics permits, facilities privileges, carrier reimbursements, and Medicaid/Medicare registrations. For a gross offense all of these actions could be justifiable, but as is the case with many reprimands, the offense may be limited, or the reprimand unwarranted.

Additionally, the record of censure does not present a comprehensive analysis of the factors surrounding the incident. As a result, the judgments of other bodies are questionable without full exploration of the circumstances which led to the initial protest. Even the most highly skilled and respected professionals are at one time or another subject to conduct review. The apprehension that, aided by the data bank, this type of inquiry could destroy a legitimate career, is warranted. Physicians are beginning to find that their efforts to avoid potentially damaging situations, or possibly litigious patients, are interfering with the level of health care which they can comfortably provide.

A tangible development is the growth of an industry dedicated to the management of medical risk, and to the defense of practitioners under examination. Health care professionals are forced to turn to legal firms for advice at the first sign of an impending disciplinary hearing or inquiry. In fact, many physicians now rely on intermediaries who have special interests or experience in representing PIDs. Medical journals are replete with advertisements publicizing the availability of these services.

In addition, one of the more recent malpractice indemnity provisions is the inclusion of a PID rider. United Physicians Insurance (UPI), a Memphis, Tennessee based risk retention group incorporated under the Federal Risk Retention Act, executes specific defense initiative assurances. According to UPI, they will reimburse policy holders defending themselves against disciplinary actions initiated by health care entities, state and federal regulatory authorities. The group will also provide a staff physician/attorney for the initial legal evaluation/advisory meeting with the insured. These types of indemnity policies are fast becoming fixtures in the insurance portfolios of American health care professionals.

The importance of early counsel cannot be stressed enough. During an October 1989 risk management seminar conducted in New York State, representatives from the Health Care Facilities Administration, The New York State Inspector General's Office, and the Office of Professional Misconduct, repeated this theme time and time again. Defensive motions must be made as quickly as possible in order to prevent the submission of potentially damaging documents or testimony. Furthermore, any delay in responding to a complaint may appear to a review board as an insubordinate act, and further impair the prospects for a favorable outcome.

In the past, physicians who had received an unfavorable malpractice judgment were penalized by an increase in premiums, or perhaps, a restriction of their medical practices. Today, the same outcome could place a professional's license in jeopardy. To protect their health care privileges, doctors must be prudent enough to identify potentially hazardous

conditions, and knowledgeable enough to seek timely effective counsel.

RICHARD S. GOODMAN, MD
S. KEITH LONDON, BS
Medical Risk Management
Advisory Corporation
285 East Main Street
Smithtown, NY 11787

1. United States Department of Health & Human Services. *National Practitioner Data Bank Guidebook*, Washington, DC, 1989, p1.

The immunization crisis in New York

TO THE EDITOR: Dr Birkhead's commentary "The immunization crisis in New York" is comprehensive both historically and in the consortium plans to address the "immunization crisis."¹ However, I was surprised that he did not mention the chilling effect of the Centers for Disease Control (CDC) Vaccine Information Pamphlets: "What You Need to Know" on physicians and other providers.

Under the requirements of the National Vaccine Injury Act (enacted in 1987 but not implemented until 1992) physicians must have patients, parents or surrogates read and sign these pamphlets (12 pages each for DPT, MMR, and polio) prior to *each* vaccination. The New York State Department of Health has informed me in response to a physician's inquiry that these must even be used in the emergency room when giving a tetanus booster! It is anticipated that CDC pamphlets for *Haemophilus influenzae* type b vaccine and Hepatitis B vaccine will be published in the near future. Physicians must make their own copies or purchase the pamphlets, significantly adding to the already high cost of vaccines.

I would urge Dr Birkhead to organize a national consortium to petition the CDC to modify (shorten) the pamphlet formats greatly and provide relief from their seemingly redundant application.

PETER B. FARNSWORTH, MD
Director, Division of Public
Health and Education
Medical Society of the State of New York
420 Lakeville Road
Lake Success, NY 11042

1. Birkhead G: The immunization crisis in New York. *NY State J Med* 1992; 92:415-417.

In reply. Many in the public health community share Dr Farnsworth's concern that the Vaccine Information Pamphlets (VIP) may be a barrier to immunization efforts. The State Department of Health has written to the Director of the Centers for Disease Control (CDC) expressing this concern and asking that both the pamphlets and the signature procedures required by CDC in the public sector be streamlined. In addition, Governor Mario Cuomo has written to Secretary Louis Sullivan of the US Department of Health and Human Services (HHS) expressing a similar concern.

The Department of Health has sought to develop data on the barrier that VIP forms may present by providing partial support for a study at the University of Rochester of the impact of the public sector signature requirement for VIPs on vaccination series completion. Also, under the provisions of the National Vaccine Injury Compensation Act, CDC will be conducting an evaluation of the VIPs. I have had a chance to review and comment on the proposed CDC protocol in my role as consultant to the Council of State and Territorial Epidemiologists. These studies should provide firm data on which to base an assessment on the impact of VIP use.

On the regulatory front, I understand that Congress has requested HHS to comment by January 15, 1993, on how the VIP process could be simplified (S. Sepe, Division of Immunization, CDC, personal communication). In addition, the American Academy of Pediatrics and other groups are continuing to push for legislative reform of the VIP process. Hopefully, these efforts will bear fruit in 1993. In the meantime, we should continue to address the numerous other barriers to immunization and primary care for children outlined in my commentary.

GUTHRIE S. BIRKHEAD, MD
Director, Immunization Program
New York State Department of Health
Corning Tower
Albany, NY 12237

Lead screening

TO THE EDITOR: We noted with interest Dr Cone's article on lead screening and follow-up in the August issue of the *Journal*.¹ We have recently concluded a study of lead testing and follow-up in the eight Pediatric Resource Centers administered by the Medical and Health Research Association of New York City, Inc, and supported by Maternal and Child Health Block Grant funds. These Centers, which operate within the outpatient departments of municipal and voluntary hospitals and in freestanding community health centers, provide primary care to children and adolescents at particularly high risk for poor health outcomes. Approximately 28,000 patients are seen and 103,000 visits generated annually. For the past eight years, studies of the quality of comprehensive care and continuity of care have been conducted.²

This year, we also examined selected preventive health measures. The sample, which was reviewed by nurses from the New York County Health Services Review Organization, was selected from the automated data system and consisted of patients with selected risk conditions including parenting problems, low birth weight and sheltered or dislocated children or families. Children had to have made at least three visits to remain in the sample and to have enrolled no longer than 18 months prior to review.

The records of all children between the ages of nine months and six years of age were examined to determine whether an erythrocyte protoporphyrin test was performed and whether follow-up blood lead levels were taken if the results were over 35 µg/dL. There

were 229 children in the sample eligible for testing and 175 or 76% of them were actually referred for testing. The test was completed, and results were present, in 148 or 65%. There were 19 cases where findings were abnormal (13%) and, of these, 14 (74%) had blood levels taken, as compared with the 43% found in Dr Cone's study. Failure to follow-up was almost equally distributed among the six centers where abnormal results were found. Although our study did not include all of the items in Dr Cone's study, we thought that our results would be of interest to readers.

LUCILLE ROSENBLUTH, MPA
President
Medical and Health Research Association of
New York City, Inc
40 Worth Street
New York, NY 10013

MILDRED A. MOREHEAD, MD
Professor Emeritus, Epidemiology and Social
Medicine
Albert Einstein College of Medicine
1300 Morris Park Avenue
Bronx, NY 10461

1. Cone DC: Lead screening and follow-up in an urban pediatric clinic. *NY State J Med* 1992; 92: 338-342.

2. Rosenbluth L, Morehead MA, Grossi M, et al: A model for evaluating the delivery of pediatric primary care services. Quality assurance and utilization review, 1991; 5:2-7.

Münchhausen syndrome

TO THE EDITOR: This letter is written to thank the *Journal* for the Clinical Conference entitled "Münchhausen syndrome" published in the July 1992 issue.¹ The case presented helped us to manage a difficult situation.

A 34-year-old black man was transferred from a nearby hospital for evaluation and treatment of Goodpasture's syndrome. He stated that two years earlier, he had presented to another hospital with recurrent hemoptysis and hematuria and had undergone renal biopsy, bronchoscopy and antiglomerular basement membrane studies. According to the patient, he had been treated with steroids, cytoxan, and plasmapheresis. On admission, the patient complained of flank pain. Our physical exam revealed a central venous catheter and his urinalysis was positive for occult blood. His previous physicians and medical records could not be located.

When this patient was presented by a medical student, the attending physician recalled a case report on Münchhausen's syndrome published the previous month in the *New York State Journal of Medicine*.¹ The patient described in the article and our patient were the same age and race and both claimed to have been fighter pilots in the Gulf war. They both had the same complaints and gave a history of similar diagnostic evaluations and treatments. Personal communication with one of the authors confirmed our suspicion that the patients were one and the same; he had not changed his name. After we confronted our patient, we learned that he

had contaminated his urine samples with blood obtained from a peripheral venous catheter. When we recommended psychiatric consultation, he immediately left the hospital against our advice.

Ifudu et al in an article entitled "Kidney-related Münchhausen's syndrome" in the *New England Journal of Medicine* suggested establishing a formal registry of patients with Münchhausen's syndrome.² Our encounter with this patient dramatically supports this recommendation. Not only does he tell a convincing story, but since he is taking steroids and still has his central line in place, physicians who care for him in the future may be led astray. A formal registry of these patients may help physicians avoid prescribing expensive, invasive, and potentially harmful diagnostic procedures and therapies. Patient confidentiality in such a registry would need to be considered.

STEPHEN P. LICATA, PhD
Medical Student-IV

LESLIE A. McCLOSKEY
Medical Student-III

CAROL L. KARMEN, MD
Division of General Internal Medicine
Department of Medicine
New York Medical College
Valhalla, NY 10595

1. Flynn J (ed): Münchhausen syndrome. *NY State J Med* 1992; 92:301-305.

2. Ifudu O, Kolanski SL, Friedman EA: Brief report: kidney-related Münchhausen's syndrome. *N Engl J Med* 1992; 327:388-389.

In reply. We appreciate the opportunity to comment on the above letter which recounts the experience of the Department of Medicine at the New York Medical College with a Münchhausen patient who undoubtedly is the same individual with whom we had prior contact.¹

Experienced clinicians are often led astray in their initial diagnostic and therapeutic approaches to this type of clinical problem because the well-researched history as offered by the patient can be thoroughly convincing. The clinician naturally assumes that the patient is telling the truth, particularly about the symptoms of a potentially life-threatening illness.

Past records that would be informative are often not immediately available, and the clinician's focus is naturally on the timely evaluation and treatment of an apparently serious medical condition. Possible inconsistencies in the medical history may be initially overlooked; an example in point would be this patient's claim to be a Navy fighter pilot, yet with a history of long-standing Goodpasture's syndrome.

When the true problem is uncovered, the patient rejects psychiatric evaluation and assistance, and promptly removes himself to another medical institution where the same or a similar scenario is repeated.

The tragedy of the Münchhausen syndrome is its inaccessibility to definitive treatment,

coupled with the ongoing repetitive exposure of the patient to invasive procedures and potentially hazardous treatments, until a catastrophe terminates the patient's life or results in serious irreversible harm. A possible means of help to these unfortunate patients is appropriate publicity of such cases to the medical community, so that potentially hazardous experiences for the patient can be minimized or entirely avoided in the future.

A registry of such patients, as suggested in your letter and also by others,² would assist hospitals and physicians, and be beneficial to the patients themselves through the avoidance of invasive procedures. Confidentiality

could be protected through anonymity in the publication of brief accounts of clinical histories; however, dissemination of such information on a regular basis to a large medical community would require periodic presentations in a major medical journal or several such journals.

In the present case,¹ the patient invariably offered the same clinical history, physical findings, and even social history. However, a potential drawback to the effectiveness of a Münchausen registry is the frequency with which such patients change their histories and physical findings, once the truth of their situations is uncovered.

Again, we are pleased to know that our report and the cooperation of the *Journal* in its publication have been beneficial to both the patient and to your institution.

BRUCE D. LOGAN, MD

JOHN T. FLYNN, MD

New York Downtown Hospital

170 William Street

New York, NY 10038

1. Flynn J (ed): Münchausen syndrome. *NY State J Med* 1992; 92:301-305.

2. Ifudu O, Kolasinski SL, Friedman EA: Kidney-related Münchausen syndrome. *N Engl J Med* 1992; 327:388-389.

SAVE THE DATE!

Long Island Region to Host New York State Public Health Association Statewide Conference on Women's Health

The Long Island region will host the New York State Public Health Association's Statewide conference on women's health on Thursday and Friday, June 24-25, 1993, at Hofstra University, Hempstead, Long Island. Panel topics are expected to include: breast cancer, cardiovascular and infectious diseases, substance abuse, adolescent health, maternal and child health, mid-life issues, aging, and violence.

Dr Mark R. Chassin, Commissioner of the New York State Department of Health, is among the many prominent keynote speakers that have accepted invitations to address the conference.

For further information, please contact Chairperson Rosemarie Guercia, MD, MPH, (516) 938-8678 or Bert Jablon, (516) 921-5174.

When others must choose: Deciding for patients without capacity

The New York State Task Force on Life and the Law. 288 pp, New York City, 1992. \$9.00 (softcover)

In 1985, the Governor brought together the New York State Task Force on Life and the Law to advance public policy in the realm where medicine and the law intersect. Over the years, the Task Force's reports on end of life issues have changed the clinical landscape in New York. Their work has inspired important legislation governing the determination of death, the withholding of cardiopulmonary resuscitation, and the appointment of a health care agent. While each of these initiatives were delicate and difficult matters, there is perhaps a no more contentious intersection of medicine and the law than the question of surrogate decision making. That is the topic of this report.

Surrogate decision making poses special ethical problems. Unlike the direct choices made by competent adults, deciding for others who have lost capacity requires that the patient's right to direct his or her care be delegated to another. This transfer of authority raises two fundamental questions. First, to whom should this authority be given? Second, what decision making criteria should govern this surrogate's delegated responsibility?

Because of these complexities, the Task Force continues to recommend that competent adults designate a health care agent under the state's health care proxy law. The Task Force suggests that patients can best protect their rights and promote their future interests by deciding in advance. The special standing of the health care agent, among other surrogate decision makers, is maintained in this proposal because of the recognition that such individuals were deliberately chosen by the patient before capacity was lost. Indeed, the Task Force describes the involvement of surrogates as a "default decision-making process" and encourages patients to complete an advance directive.^{1(p x)}

Although the law has traditionally given competent patients a wide breadth in directing their own care, the latitude of surrogate decision makers has been more narrowly constricted. That is, while competent patients have the right to make "foolish choices," the surrogate's decisions must come under closer scrutiny. This limitation of the surrogate's power has important consequences, given today's medical technology. Many of the most discretionary choices at the end of life are left to surrogates when the patient cannot directly participate in the decision. While the power of surrogates must be carefully considered, the surrogate's severely constrained authority has made them ill-equipped to grapple with the dilemmas posed by advanced medical technology at the end of life.

The Task Force has taken the important step of recognizing the difficulty of surrogate decision making in New York by voicing concern about "the legal vacuum that surrounds many surrogate decisions today."^{1(p 237)} In a scholarly and cogent review of the case law, the Task Force illustrates how the doctrine of clear and convincing evidence came to dominate surrogate decision making in New York. More importantly, the

report notes how this stringent criterion has failed to meet the needs of the incapacitated. This proposal seeks to redress their risk of overtreatment when "clear guidance" about treatment preferences do not exist and of undertreatment when consent is needed for comprehensive medical care.

Under this proposal, surrogates would be authorized to make treatment decisions for incapacitated patients without clear and convincing evidence of the patient's wishes. These decisions would be appropriate after the attending physician finds that the patient lacks capacity and this determination is confirmed by another health care provider. Surrogates would be instructed to invoke a substituted judgement standard of decision making when some knowledge of prior wishes are known or to use a best interest standard when no information is available. The Task Force's definition of best interest is sufficiently broad to allow surrogates to consider how a treatment might affect the patient's functional or health status, survival, dignity, uniqueness, and personal values.

This departure from a clear and convincing standard is matched by the range of decisions that surrogates would be allowed to make. Unlike the earlier do-not-resuscitate legislation which empowered surrogates to make choices which were limited to decisions about resuscitation, this proposal would expand the domain of surrogate decision making to include all treatment decisions not just those about life-sustaining treatments.

The Task Force proposes that surrogate decision making be regulated within institutions by state-mandated multidisciplinary "bioethics review committees." Access to these committees would be open to health care providers, patients, and surrogates. These committees would be required to adhere to state policies on decision making procedures, access, and patient confidentiality.

Unlike conventional ethics committees, bioethics review committees would be empowered to approve decisions made by a surrogate to withhold or withdraw life-sustaining therapy when a treatment imposed an undue burden upon a patient who was neither terminally ill nor in a persistent vegetative state. In these scenarios, the committee could either approve a decision to forgo a life-sustaining therapy or prevent the surrogate from consenting to the implementation of such a decision without the intercession of the courts. Bioethics review committees would also serve to review and approve decisions to forgo life-sustaining therapies for incapacitated patients who were without surrogates. Although the bioethics review committee would become the principal locus for the regulation of institutional surrogate decision making, the Task Force notes that the existence of these committees would not prevent families from "bypassing" them "and seeking judicial intervention at any time."^{1(p 152)}

As the proposal requires that institutions develop bioethics review committees, it also places new responsibilities on physicians and other health care providers in New York State. The Task Force recommends that the attending physician, with the "concurrence" of a second physician, have the authority to make major medical decisions for the adult patient

who lacks both capacity and a surrogate. This authority is advanced so as to ensure that this isolated and vulnerable population receive "timely and appropriate care."^{1(p xiii)} Decisions to forgo life-sustaining therapy for an isolated and incapacitated patient would require approval by a bioethics review committee. This decision, however, could be authorized by the attending and concurring physicians, if they believe "in accord with accepted medical standards and to a reasonable degree of medical certainty, that the patient will die within a short time even if the treatment is provided."^{1(p 171)} The bioethics review committee would only review these "imminent death cases" if the attending and consulting physician failed to reach agreement on a course of action.

The report also highlights the obligation of health care professionals to provide adequate and effective pain control at the end of life, "even when such treatment may hasten the patient's death." They rightly recommend that the profession "accord pain control a higher priority in medical practice and education." The alleviation of pain is properly distinguished from euthanasia, which continues to be prohibited.^{1(p 223)}

Surrogate decisions about artificial nutrition and hydration are also addressed. This proposal departs from the health care proxy legislation by failing to distinguish between artificial nutrition and hydration and other life-sustaining therapies. Unlike the health care proxy law, where the agent is only empowered to make decisions about artificial nutrition and hydration if the agent knows the patient's wishes about these interventions, surrogates under this legislation would be able to withhold or withdraw artificial nutrition and hydration without specific knowledge of the patient's wishes. In an assertion which would logically expand the authority of the health care agent, the Task Force asserts that the procedural safeguards proposed for "other life-sustaining treatments are appropriate and sufficient for decisions about artificial nutrition and hydration."^{1(p 219)}

As the proposal would clarify surrogate decision making for adult patients, it also addresses decisions made on behalf of children and emancipated minors. The task force suggests that a parent or court appointed guardian have the authority to withhold or withdraw life-sustaining therapy if they adhere to the same guidelines described for adult surrogate decision making. A minor with decision making capacity would, however, need to consent to a decision to forgo such treatment. Emancipated minors deemed to have decision making capacity would be allowed to forgo life-sustaining therapy if they complied with standards for adult surrogate decision making and had the approval of the bioethics review committee.

While the report makes for good reading, it is unclear whether the proposal would make good public policy. As a response to current New York law which embraces a clear and convincing standard of decision making and which narrowly constricts the domain of surrogates' authority to decisions about resuscitation, this proposal represents a clear improvement. Politics and antecedent case law would seem to dictate that such a report would be responsive in tone. Nevertheless, it is unfortunate that the Task Force did not use this opportunity to place state law into the national mainstream where the natural authority of family members who serve as surrogates is rightly recognized and acknowledged.

Although the Task Force notes that, "by and large, decisions made in accord with the proposed law will be private bedside decisions by those closest to the patient,"^{1(p xii)} the provision for regulatory bioethics review committees seems to undermine the deference which should be accorded to family members who serve as surrogates. These committees might productively serve to mediate disputes or to meet needs of isolated and incapacitated patients if there were sufficient attention paid to due process considerations.

The suspicion that families and physicians would fail to serve the needs of patients and loved ones, however, seems counterintuitive. Mandated approval of decisions to withdraw or withhold burdensome life-sustaining therapy from patients who are neither terminally ill nor permanently unconscious seems to improperly question the standing and judgment of family and medical professionals. This skepticism seems particularly unfounded when surrogate and physician are in agreement about a course of action. As a vehicle to safeguard the vulnerable patient, it seems unlikely that an institutional bioethics review committee could accomplish more than familial intimacy and professional virtue can. This level of review seems to legislate for the exception rather than the rule. Generally families are motivated by affection and concern for their loved one, not a conflict of interest.

Committee review of decisions to withhold or withdraw life-sustaining treatments from patients who are neither terminally ill nor permanently unconscious may paradoxically erode the authority already given to surrogates under existing do-not-resuscitate (DNR) laws.² While a DNR surrogate is currently authorized to forgo resuscitation in a demented patient because this might impose a disproportionate burden, the surrogate under this proposal would need the approval of the bioethics review committee because dementia is neither a terminal condition nor a state of permanent unconsciousness.

The institutionalization of some surrogate decisions may in fact threaten what we value in the doctor-patient relationship. The emergence of bioethics review committees has the potential to displace medical professionalism by changing the physician's understanding of his or her role and obligations. It would be unfortunate if committee meetings and not the bedside were seen as the place where thoughtful and heartfelt deliberations about patients' needs took place. The regulatory oversight of the committees is especially confounding given that the Task Force seems to acknowledge the physician's role in discerning physiologic futility in cases of "imminent death."

The erosion in the doctor-patient relationship might be tolerable if we could be assured that the alternatives would better serve incapacitated patients. While there is a limited role for bioethics review committees in the care of the isolated and incapacitated patient, it remains to be seen whether they would promote better decisions than the ones made by concerned family and physicians when there is a natural surrogate. Others have studied the correlation of treatment preferences among surrogates, patients, and physicians.^{3,4} Before we embark on the institutionalization of many end-of-life decisions, a similar investigation should be conducted that determines how well a bioethics review committee does in approximating the wishes of capacitated patients. While the choices made by family and physicians don't correlate as well with the choices of patients as we might like, we might be surprised to learn that natural surrogates and physicians still do better than uninvolved and sequestered committees.

Distinguished reports like this one have interest beyond the clinical setting because they are reflective of important societal trends. This is especially true of the Task Force's work because of the diversity of its membership. In this larger context, the report's regulatory tone tells us that we trust neither family nor professionals. Indeed, it sadly illustrates our society's growing distrust of itself.

JOSEPH J. FINS, MD
Associate for Medicine
The Hastings Center
255 Elm Road
Briarcliff Manor, NY 10510
Instructor in Medicine
Cornell University Medical College
New York, NY 10021

1. The New York State Task Force on Life and the Law. When others must choose: deciding the patients without capacity. March 1992.

2. Moreno JD. Conference speaker at "When others must choose: an examination of the New York State Task Force on Life and the Law Proposed Legislation for Surrogate Decisionmaking." The Metropolitan New York Ethics

Committee Network at the New York Academy of Medicine. October 15, 1992.

3. Uhlmann RF, Pearlman RA, Cain KC: Physicians' and spouses' predictions of elderly patients' resuscitation preferences. *J Geront* 1988; 43:M115-121.

4. Uhlmann RF, Pearlman RA: Perceived quality of life and preference for life-sustaining treatment in older adults. *Arch Intern Med* 1991; 151:495-497.

A long lost manuscript on the Peruvian bark

A Plain Treatise on the Peruvian Bark ("The Stanitz Manuscript"). A Late Seventeenth or Early Eighteenth Century Anonymous Manuscript Account of the Jesuits' Bark Published in its Original Latin Text with a Translation, Introduction and Notes. By Saul Jarcho, MD. 116 pp. Boston. The Francis A. Countway Library of Medicine, 1992. \$19.95 (hardcover)

Since it was first brought to Europe in the early 17th century, Peruvian bark, or Cinchona, has been the object of much study. In part this is due to the fact that it was the first really effective treatment for malaria and remained so until replaced by more effective drugs a few decades ago. Most scholars now discount as apocryphal, the story that the bark cured the Countess of Cinchona, the first wife of the Viceroy of Peru. Yet, the synonym Cinchona has stuck for three centuries. What is more certain is that the efficacy of the bark in treating intermittent fevers was first described by a Spanish missionary, Fray Antonio de la Calancha, in 1633. The long and interesting story of Cinchona and its alkaloids was detailed in the pages of the *Journal* in 1988 by the late Leonard Jan Bruce-Chwatt ("Cinchona and its alkaloids: 350 years," 1988; 88:318-322). As he pointed out, as soon as the efficacy of the bark became known, the race to secure its sources got underway. By the late 18th century, the efficacy of the drug was well established, aided in part by Robert Talbor's successful treatment of King Charles II.

In the volume under review, Saul Jarcho, MD, a renowned medical historian and linguist, has added a new and exciting chapter to our knowledge of Peruvian bark by translating from Latin a long lost, late 17th or early 18th century manuscript on the subject. The manuscript in question lacks a title page and author. However, from the writings cited, Dr Jarcho was able to place its composition in the late 17th or early 18th century. He was also able to determine that the author was probably a physician with considerable experience in the use of the bark and well informed about what the leading men of medicine of his era had to say about it.

The importance of this book lies in the fact that it presents the heretofore unknown views and experiences of a writer who lived at the time that Cinchona was first being widely used in Europe. It fills in the story of Peruvian bark, presents one man's learned critiques of contemporary thought on the subject and provides an added glimpse into the world of late Renaissance medical writing (Fig 1).

In a 19-page introduction, Dr Jarcho describes the known history of the manuscript, its physical characteristics, the editorial methods of the author, the author and his opinions, the evidence used to approximately date the manuscript and its position in relation to the history of medicine and the history of Cinchona. Finally, in a speculative section entitled, "A Possible Cartesian Connection," Dr Jarcho discusses its possible connection to the followers of René Descartes (1596-1650).

The task of translating this manuscript must have been a formidable one, given that it is written in a cursive hand. Dr

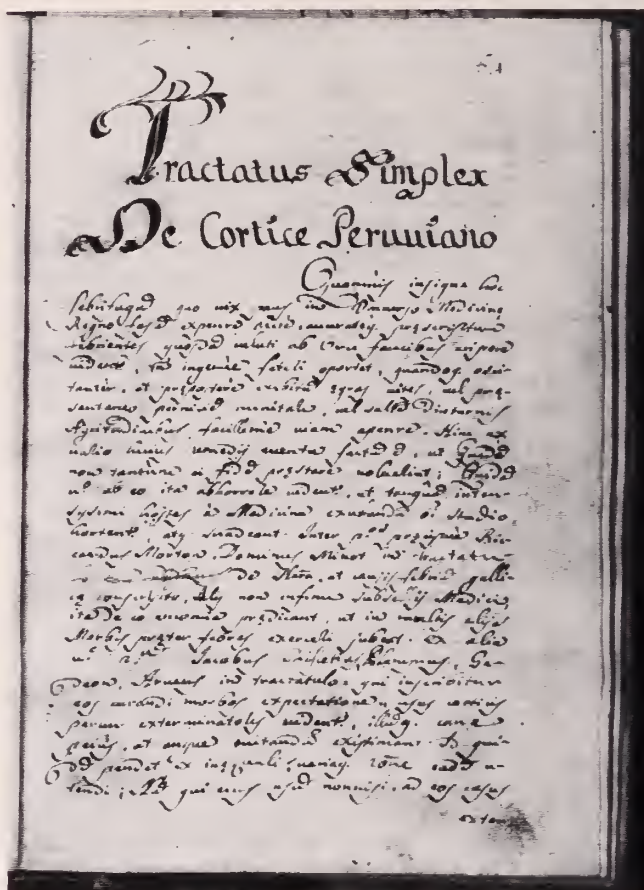


FIGURE 1. Folio 64r, the first leaf of the essay (courtesy of The Francis A. Countway Library of Medicine).

Jarcho not only provides a full translation in contemporary English but also reproduces the original Latin version in printed form on the opposite page. Notes to both the Latin and English texts are provided as well as separate indexes of authors and subjects mentioned. Two pages of principal references are also included, some of which were cited by the author of the original Latin text.

Dr Jarcho has successfully brought to light an important and interesting historical document. It not only increases our knowledge of early views of Peruvian bark, but more importantly better informs us about medical concepts of other times. The book may be ordered from Science History Publications-SA, PO Box 493, Canton, MA 02021.

PASCAL JAMES IMPERATO, MD
Editor

DISORDERS OF LEARNING IN CHILDHOOD

By Archie A. Silver, MD, and Rosa A. Hagin, PhD. 683 pp, illustrated. New York, John Wiley and Sons, 1990. \$65.00 (hardcover)

A major problem in treating children with learning disorders is that of linking the perspectives and contributions of several disciplines. Usually, one discipline dominates the diagnostic and therapy decisions. Archie A. Silver and Rosa A. Hagin have successfully blended the disciplines of medicine, education, psychiatry, and psychology in their book *Disorders of Learning in Childhood*. Silver and Hagin have worked together for over 40 years in providing clinical services to children with learning disorders, in conducting research, and in producing assessment and teaching instruments. Their book reflects the lifelong collaboration of a child psychiatrist (Archie Silver) and a clinical psychologist (Rosa Hagin). Their remarkable teaming over many years provides a unique and unusual quality to this book. Much of their work was conducted in the Department of Psychiatry at New York University School of Medicine. However, their collaboration continued when Dr Silver became Professor of Psychiatry and Director of Child and Adolescent Psychiatry at the University of South Florida, College of Medicine, and Dr Hagin became Professor of Psychology and Director of the School Consultation Center at Fordham University.

Silver and Hagin's underlying tenet is that understanding and treating learning disorders in children requires a comprehensive perspective that integrates biological, psychological, educational, and social perspectives. This book offers a clinically based classification of learning disorders, it advances general principles of diagnosis and management, and delineates the categories of learning disorders most frequently seen in clinics and classrooms. It also offers specific and practical recommendations for the management of various disorders.

The book is organized into four major sections. Part One is a general view of learning disorders and contains four chapters; the problems of definitions (chapter 1), clinical classifications of disorders of learning (chapter 2), a review of studies of subgroup patterns of neuropsychological dysfunction (chapter 3), and a discussion of prevalence estimates of the various disabilities (chapter 4). Part Two presents principles of management and contains six chapters: principles of educational and psychological diagnosis (chapter 5), principles of psychiatric and neurological diagnosis (chapter 6), principles of educational remediation (chapter 7), medications affecting learning and memory (chapter 8),

principles of psychotherapeutic management (chapter 9), and the prevention of learning disorders (chapter 10). Part Three considers clinical patterns of disorders of learning within six chapters: specific language disability (chapter 11), effects of poverty, cultural differences, and inappropriate stimulation (chapter 12), attention deficit hyperactivity disorder (chapter 13), organic disorders (chapter 14), Tourette's syndrome (chapter 15), and autism (chapter 16). Part Four has only one chapter, and it looks at future directions for service and research.

There are three valuable appendices, reflecting both the psychiatric and psychological perspectives: Code of Fair Testing Practices in Education (appendix A), an outline of mental status evaluation (appendix B), and an outline for neurological evaluation (appendix C).

The uniqueness of this book is that it reflects the collaboration of two scholars who have dedicated their careers for over 40 years to understanding and providing services to children with a variety of learning disorders. Any review of the significant contributions to the field of learning disabilities, for example, reveals the research of Archie Silver and Rosa Hagin. The results of their work consistently appear in the psychiatric, psychological, and educational literature.

The process of establishing a diagnosis is comprehensively presented in several chapters in Part One, from the educational, psychological, and psychiatric perspectives. This discussion includes thorough coverage of research, tests, and procedures from each of these perspectives. The discussion also includes a wealth of information that can assist practitioners from several disciplines in establishing a diagnosis. The discussion of underlying principles spans the educational and medical perspectives and includes a survey of traditional and new approaches to the teaching of reading and language arts. Another chapter offers a thorough presentation of medications and how they affect the brain, learning, and memory. The review of research studies on the effects of medications should be especially helpful to physicians and psychiatrists.

Emotional and behavioral problems often accompany learning disorders, and these problems are viewed as family problems. One chapter offers a practical guide for providing therapy for the child, parents, and families, through psychotherapy.

Children at risk for learning failure and ways to prevent learning disorders from occurring through teaching is the subject of an entire chapter. The authors have collaborated for many years in finding ways to identify and teach young children at risk,

and this body of information is presented in the chapter on prevention.

The chapter on specific language disability is encyclopedic in its review of the literature and spans early studies and contemporary research. The chapter on attention deficit disorders provides an excellent overview of a topic of much current interest. Attention deficit disorders and attention deficit hyperactivity disorders are presented from the perspective of the school, the psychiatrist, and the psychologist.

A separate chapter deals with Tourette's syndrome. The thorough discussion of this syndrome includes general information, a review of medications, and specific suggestions for teaching. This information should be of help to physicians, psychologists, and school personnel. Another chapter deals with autism. The number of children identified as autistic is increasing, and knowledge about the causes, and the medical and educational management of this condition is undergoing change. The information on autism brings the reader up-to-date on the nature and treatment of this disorder.

Disorders of Learning in Childhood is clearly written, up-to-date in its information, provides ample research on each topic, and most importantly integrates the medical, educational, psychological, and educational perspectives. The many brief cases in each chapter serve to illustrate and clarify the topics under discussion.

JANET W. LERNER, PhD
Professor of Special Education
Northeastern Illinois University
5500 N. St Louis Avenue
Chicago, IL 60625

THE PROSTATE BOOK: SOUND ADVICE ON SYMPTOMS AND TREATMENT

By Stephen N. Rous, MD. 285 pp. New York, WW Norton and Company, 1992. \$22.95 (hardcover)

Dr Stephen N. Rous is a well known and experienced educator who has won wide acclaim for his expertise. He has brought his considerable talents and practical experience to bear in writing this informative text. Within its pages, he clearly and comprehensively addresses all aspects of the prostate and its dysfunctions. He reviews the normal anatomy and function of the prostate: prostatitis, benign enlargement (so-called BPH), and cancer. One chapter guides the reader through the mysteries of how a physician establishes the diagnosis of a prostate problem and what techniques are available for the evaluation of each diagnosis. A unique chapter is entitled, "What you (the pa-

tient) can anticipate at each step along the way." The practice of medicine is an art as well as a science and this chapter allows the reader to get some appreciation of that fact. Thorough discussions of the various surgical procedures and their complications are included. Radiation therapy is also addressed.

Throughout the book there are excellent illustrations and photographs which nicely complement the text. In this updated version of a previously published book, Dr Rous brings to the reader the current state of the art. His final chapter is a compilation of all the latest information regarding each of the subjects covered in the earlier chapters. Among many other subjects included are prostate specific antigen (PSA), ultrasound examination of the prostate, non-surgical treatment of BPH, the controversy involving an open operation for the prostate as opposed to a transurethral resection, balloon dilation as a treatment for benign enlargement, hyperthermia, and laser surgery. When this final chapter is combined with the basics of the preceding chapter, the textbook becomes an invaluable and readable guide for any person interested in a greater understanding of the prostate. Although this is primarily directed at non-physicians, many non-urollogic physicians will also find it enjoyable and informative. This is a full-length textbook of 270 pages. It is well worth the time and effort for the interested reader to study from the first to the last page. I recommend it to my patients, first-year residents, medical students, urologic nurses and non-urollogic colleagues.

RICHARD J. MACCHIA, MD
Professor and Chairman
Department of Urology
State University of New York Health Science
Center at Brooklyn
445 Lenox Road
Brooklyn, New York 11203

BLOOD ATLAS AND SOURCEBOOK OF HEMATOLOGY

By Carola T. Kapff, SH, and James H. Jandle, MD. 158 pp, illustrated. Boston, MA, Little Brown and Company, 1991. \$95.00 (hardcover)

Careful scrutiny of the peripheral blood and bone marrow are integral components of the process of evaluating patients with hematologic disease. Indeed, these topics are often among the openers in textbooks of hematology and are emphasized in training programs. To this end, an atlas should serve as a tool of easy learning coming in handy in unraveling a blood disorder. When shopping for an atlas, the hematologist's wish list includes: clear illustrations, as close to the real microscopic picture as possible, with emphasis on oil immersion photographs, alongside which are meaningful descriptions of the

abnormalities, their differential diagnoses, and a word or two about their pathophysiology. It should be a quick guide to most, if not all, morphologic abnormalities one encounters in everyday practice. To a great extent, Kapff and Jandl's atlas fulfills these wishes: Beginning with pitfalls in peripheral smear and bone marrow specimens, it goes on to describe and illustrate most hematologic disorders that come to mind. The photographs are clear, posing a challenge to many other atlases, and the narrative is pertinent answering questions that come to mind as one peeks through the eyepiece of the microscope. Their writing style is inviting, seasoned, and metaphorical at times, making difficult terms easier to comprehend even for those who do not make hematology an everyday trade. The final section addresses the cellular morphology of body fluids, an area which has received little attention in many texts but which is of great significance to the practicing physician. The chapter on glossary and thesaurus is likely to be a refuge for those struggling to keep up with newer terms and a comfort for those who need to be reminded of the older ones. However, in some areas the atlas is found wanting: the myelodysplastic disorders were telescoped in one page and chronic myelomonocytic leukemia did not find a place in the book. Some significant tumor markers as CD5 in chronic lymphocytic leukemia and Tdt in lymphoplasmic lymphoma were omitted. It would be nice to see a reference to disorders that manifest Reed-Sternberg-like cells in conditions other than Hodgkins's disease. A list of CD markers may be helpful in complementing the morphologic picture and are not quite beyond the scope of the atlas. Kapff and Jandl state that theirs is primarily a photographic atlas and it is. They have achieved their objective with a great deal of success. Their atlas is a worthwhile investment and should be on the shelf of not only the hematologist but also the internist, the medical student, and the laboratory technologist. On all these bookshelves, Kapff and Jandl is going to be a valuable tool and is not expected to gather dust.

A. Z. MAKARY, MD
Chief, Section of Hematology
Geisinger Medical Center
Danville, PA 17822

IF A PARTNER HAS AIDS: GUIDE TO CLINICAL INTERVENTION FOR RELATIONSHIPS IN CRISIS

By R. Dennis Shelby, PhD. 277 pp. Binghamton, NY, Harrington Park Press, 1992. \$14.95 (softcover)

This book is a compilation of stories about partner couples in varying stages of human immunodeficiency virus (HIV) infection. The stories and vignettes encompass every aspect of this infection including

family, work, social aspects, and public and partner responses. The purpose of this effort appears to be to characterize and categorize the large variety of responses and emotional aspects of infection.

The author explains to us that this book is the result of years of working with couples as a therapist. The author appears knowledgeable about psychoanalytic therapy and sensitive to the issues he discusses. In his acknowledgment, there is a hint that this work may have been a dissertation and the style of writing supports that impression.

The book is helpful to anyone wanting to know what persons with HIV infection and those around them go through in various stages of the infection. The brief patient histories are augmented and organized by a classification system described by the author and used to illustrate the stages of emotional responses. Shelby has had much experience.

This work augments the social literature about responses to serious disease with the emphasis on HIV infection. To the physician who works with HIV-infected patients, this anecdotally written book will offer new insights into the problems and concerns of patients and couples. The insight provided is uniquely personal and intense.

The contents of the book include a thorough literature search as indicated both by notations in the text and the extensive list of references. The author describes his method of gathering data and originates a "staging" system. The staging system is somewhat cumbersome with the larger stages such as "confirmation," "long haul," and "fever pitch," further subdivided into smaller sections such as "this is real," "the game plan," "revelation/negotiation," "fever pitch," "balancing," "renewal," and "derailment." This classification system becomes redundant and confusing. In the Foreword, Constance Goldberg writes "Shelby has taken a microscope to the relationships he has studied. We read again and again of the comfort and soothing offered from one partner to another."

The repetition is more suitable to dissertation writing than to effective textbook use. Many of the brief anecdotal stories stand on their own, and the effort to insert every one into a classification system is occasionally tiresome to the reader. Although the classifications are appropriately descriptive, the reader does not finish the book with a cohesive flow of the classification system used. If the classification system is being included only to augment the impact of the vignettes, perhaps the author has succeeded in making his images more vivid.

The book ends with a theoretical discussion and some information for clinicians working with HIV-infected persons. This effort is helpful and informative. There are other texts which deal with the psychosocial issues confronting HIV-infected indi-

viduals and those around them, but probably none are written in the personal style of this book. This text will be of clear benefit to those who work closely with HIV disease. The author states that "my ultimate hope is that the effort provides helpful knowledge." I believe that he has accomplished this goal.

RICHARD SADOVSKY, MD, MS
State University of New York
Health Science Center at Brooklyn
450 Clarkson Ave, Box 67
Brooklyn, NY 11203

ADOLESCENT HEALTH CARE: A PRACTICAL GUIDE

By Lawrence M. Neinstein, MD. 1,089 pp, illustrated. Baltimore, MD, Urban and Schwarzenberg, 1991. \$62.00 (hardcover)

Are there enough problems unique to the adolescent to warrant a large textbook such as *Adolescent Health Care: A Practical Guide*? If I was not certain about this before reading this excellent book, I am now and the answer is an emphatic YES. It is written for all health care professionals, including pediatricians, family practitioners, nurses, and nurse practitioners who are involved in the care of the adolescent. Dr Lawrence S. Neinstein and the co-authors of this second edition of *Adolescent Health Care: A Practical Guide* are eminently qualified to produce a book of such scope and depth and they have succeeded splendidly.

The authors' approach each medical concern by delineating the areas in which the diagnosis or problem may be different in the adolescent as compared to the child or adult. This approach is crucial to the understanding of adolescent medicine. The outline format used throughout makes this book not only easy to read but also allows for rapid reference to the important facts and recommended management of the subject or illness in question.

Other features of this book that make it particularly useful to the health care professional include up-to-date bibliographies after each chapter, a large section on general references for many chronic diseases and an extensive state by state listing of community resources dealing with many of the problems relevant to the adolescent.

The quality, accuracy, and clarity of the books' contents is extremely high, with a few minor exceptions. In the chapter "Obesity," no mention is made of the importance of aerobic exercises. Under treatment for obesity, why even list drastic procedures such as gastric balloon and gastrointestinal surgery? This chapter concludes with five steps to prevent adolescent obesity, two of which make no sense at all to this reviewer. These are delaying cereals until three or four months of age, and moderate weight gain in the last trimester of pregnancy. Does this weight gain refer

to the pregnant adolescent or does it refer to the mother of the adolescent?

In the chapter, "Cardiac Risk Factors and Hyperlipidemia," it states that the prevention of adolescent obesity requires curbing obesity during the first year of life. Many studies have shown that there is very little relationship between weight gain during infancy and obesity later on in life.

While reading this volume I was reminded of a classroom discussion during one of my college courses in English about how language reflects cultural values. As examples, the English language has a tremendous number of words meaning money, while the Eskimos have many different words describing snow. After finishing the chapter on drug use and abuse, I learned that there are 18 street name words for marijuana, and 13 each for cocaine and heroin, a rather sad commentary on our present day values.

I can enthusiastically recommend *Adolescent Health Care* to all those who are responsible for the health care of the adolescent. This book is a valuable addition to the medical literature, and I commend Dr Neinstein and his colleagues on a job well done.

ALVIN N. EDEN, MD
Associate Clinical Professor of Pediatrics
New York Hospital-Cornell Medical College
Chairman, Department of Pediatrics
Wyckoff Heights Medical Center
374 Stockholm St
Brooklyn, NY 11237

THE DEMENTIAS: CROSSROADS BETWEEN NEUROLOGY AND PSYCHIATRY

By Makram Girgis, MD, PhD, and K. Harris. 187 pp, illustrated. St Louis, MO, Warren Green Inc, 1992. \$27.50 (softcover).

The title, subtitle, introduction, and text do not meet at the same crossroads. The authors highlight the clinical aspects of dementias, including both the neurological and psychiatric components, in a most cursory way. Ten of the chapters deal with the various components of the major neurotransmitter systems with particular emphasis on the glutamate system. Although these chapters are fairly lucidly written, most references are from the 1960s and 1970s with only a few in the early 1980s.

The last two chapters deal with neurotransmitter disturbances in patients with psychiatric disorders and with Alzheimer's disease and related dementias. In discussing the evaluation of dementias, magnetic resonance imaging techniques are not even mentioned. Again there are only two references from the late 1980s and these are omitted from the bibliography.

The authors target this books for "neuroscientists." However, most would probably be well versed in such material. For the clinician, there is insufficient

attention to linking the basic science with the clinical issues. Most importantly, this is a dated book, given its 1992 copyright date and its references harkening back ten to twenty years ago.

JAY E. SELMAN, MD
Clinical Professor of Neurology
and Pediatrics
New York Medical College
121 Smith Ave
Mt Kisco, NY 10549

MULTIGENERATIONAL FAMILY THERAPY

By Davis S. Freeman, DSW. 398 pp. Binghamton, NY, Haworth Press, 1992. \$24.95 (softcover)

Physicians, even those whose specialty is not Family Medicine, have long been aware of the impact of families on individual patients. Families are the often unseen forces that support and motivate a patient for treatment; or, they may create a countervailing force that impedes successful treatment. Consequently, medical professionals are compelled to figure out, often in vitro, their own renditions of family therapy. On the other hand, many of their colleagues in the field of psychology, after devoting decades of delving into patients' individual psyches, have only recently come up for air and are widening their lenses to include family systems. The result has been a growing family therapy movement, and a vast literature.

Dr Freeman, Professor of Social Work at the University of British Columbia, in Vancouver, Canada, and a prominent family therapist, has written an outstanding book that has great relevancy for physicians. First, his text offers a concise and lucid description of the process for physicians who refer or consider referring their patients to family therapy and who are curious to know more about this particular discipline. Second, the knowledge derived from reading about multigenerational family systems will deepen the physician's understanding of the patients with whom he or she works. Lastly, physicians might find the interviewing techniques used by the author applicable to their practice.

The title refers to the idea that cognitive and emotional patterns of families are influenced by the experiences of previous generations. Freeman demonstrates how discovering these family legacies—both the events and the unique meanings that people attach to the events—leads to an understanding of the current functioning of the family. He then shows how the clinician uses this material in the therapy. As important as the descriptions of his therapeutic strategies and techniques, are the descriptions of the therapeutic environment that he establishes with his patients. It becomes apparent that a welcoming, empathic, and respectful environment aug-

ments and propels the course of the treatment.

As with the best works of this kind, the fact that it is an excellent "how to" book for psychotherapists does not detract from its importance for allied professions. Unlike the arcane, ponderous, and jargon-filled approaches of many psychotherapy texts, Dr Freeman's work is concise and lucid. He illustrates his theoretical segments with poignant examples from his practice. Conversely, in the later chapters, when verbatim clinical transcripts are used, the author annotates the text with useful theoretical interpretations of what is occurring, and explanations for why he has chosen particular clinical interventions.

His talents as a clinician are matched by his intelligence as a writer and educator.

The well-organized text begins with the principles upon which family therapy is based. Freeman then focuses on the theoretical underpinnings of multigenerational family therapy. Before launching into a description of family therapy, he devotes a chapter to the examination of two issues that are crucial to the work and which will be useful to all professionals who work with families. The first is the therapist's family emotional system, and the second is the larger professional system in which the therapist and family are located.

Freeman gives the reader a solid understanding of the actual work in the chapters devoted to family therapy's various phases (eg, beginning, middle, end) and subdivisions (eg, couples, with children, siblings). The alternations between verbatim text and commentary are skillfully crafted. Even someone with little knowledge of family therapy will grasp what is happening; aspects of the knowledge gained in these chapters can easily be transposed to one's professional work.

MIMI MEYERS, MSW

Ackerman Institute for Family Therapy

149 E 78th St

New York, NY 10021



Julius Bell, MD, Hollywood, Florida. Died September 8, 1992; age 90. Dr Bell was a 1927 graduate of the University of Maryland School of Medicine, Baltimore. He was a Diplomate of the American Board of Otolaryngology. He was a Fellow of the American College of Surgeons. His memberships included the American Academy of Otolaryngology, the American Academy of Facial Plastic and Reconstructive Surgery, the Pan American Medical Association, the New York County Medical Society, and the Medical Society of the State of New York.

Calogero Bonadia, MD, Massapequa. Died July 23, 1992; age 83. Dr Bonadia was a 1936 graduate of the Università Degli Studi Di Bologna, Facoltà Di Medicina E Chirurgia. He was a Diplomate of the American Board of Ophthalmology. He was a Fellow of the International College of Surgeons and the American College of Surgeons. His memberships included the American Academy of Ophthalmology and Otolaryngology, the Pan American Association of Ophthalmology, the Kings County Medical Society, and the Medical Society of the State of New York.

Joseph R. Briamonte, MD, Bronx. Died May 15, 1992; age 80. Dr Briamonte was a 1932 graduate of Georgetown University School of Medicine, Washington, DC. His memberships included the Bronx County Medical Society and the Medical Society of the State of New York.

Paul M. Clark, MD, Albany. Died July 22, 1992; age 77. Dr Clark was a 1915 graduate of the State University of New York Upstate Medical Center, Syracuse. He was a Diplomate of the American Board of Orthopedic Surgery. He was a Fellow of the American College of Surgeons. His memberships included the American Academy of Orthopaedic Surgeons, the Albany County Medical Society, and the Medical Society of the State of New York.

Henry Cohen, MD, Brooklyn. Died August 31, 1992; age 92. Dr Clark was a 1926 graduate of State University of New York Health Science Center at Brooklyn, New York. He was a Diplomate of the American Board of Pediatrics. He was a Fellow of the American Academy of Pediatrics. His memberships included the New York Pediatric Society, the Kings County Medical Society, and the Medical Society of the State of New York.

John A. D'Anna, MD, Staten Island. Died August 29, 1992; age 70. Dr D'Anna was a 1922 graduate of the Georgetown University School of Medicine. He was a Diplomate of the American Board of Surgery. He was a Fellow of the International

College of Surgeons and the American College of Surgeons. His memberships included the New York Society for Cardiovascular Surgery, the Richmond County Medical Society, and the Medical Society of the State of New York.

Barbara DeBetz, MD, New York City. Died April 28, 1992; age 43. Dr DeBetz was a 1970 graduate of the University of Miami School of Medicine, Florida. She was a Diplomate of the American Board of Psychiatry and Neurology. Her memberships included the Academy of Medicine, the American Psychiatric Association, the American Medical Women's Association, the New York County Medical Society, and the Medical Society of the State of New York.

Elizabeth W. DeOsepel, MD, New York. Died July 7, 1992; age 94. Dr DeOsepel was a 1926 graduate of Pecs Tudományegyetem Orvostudományi Fakultás, Pecs. Her memberships included the New York County Medical Society and the Medical Society of the State of New York.

Irving Dribben, MD, Albany. Died December 24, 1991; age 89. Dr Dribben was a 1943 graduate of Albany Medical College of Union University. He was a Diplomate of the American Board of Psychiatry and Neurology. His memberships included the American Psychiatric Association, the Albany County Medical Society, and the Medical Society of the State of New York.

John Filippone, MD, Albany. Died August 3, 1992; age 84. Dr Filippone was a 1934 graduate of the Albany Medical College of Union University. He was a Diplomate of the American Board of Internal Medicine. He was a Fellow of the American College of Cardiology and the American College of Physicians. His memberships included the Albany County Medical Society and the Medical Society of the State of New York.

Emery I. Fried, MD, Nashua. Died August 16, 1992; age 84. Dr Fried was a 1938 graduate of the Université De Paris Faculté De Médecine. He was a Fellow of the American Academy of Family Practice. His memberships included the Bronx County Medical Society and the Medical Society of the State of New York.

Bordan Garbowski, MD, Utica. Died August 19, 1992; age 85. Dr Garbowski was a 1932 graduate of the Uniwersytet Jana Kazimierza Wydział Lekarski, Lwów-Lemberg. He was a Diplomate of the American Board of Family Practice. He was a Fellow of the American Academy of Family Practice. His memberships included the Academy of Medicine, the

Oneida County Medical Society, and the Medical Society of the State of New York.

William Georgi, MD, Colden. Died July 23, 1992; age 75. Dr Georgi was a 1943 graduate of the University of Buffalo School of Medicine, Buffalo. He was a Diplomate of the American Board of Physical Medicine and Rehabilitation. His memberships included the Erie County Medical Society and the Medical Society of the State of New York.

William C. Gillick, MD, Niagara. Died February 12, 1992; age 80. Dr Gillick was a 1938 graduate of McGill University Faculty of Medicine, Montreal. He was a Diplomate of the American Board of Obstetrics and Gynecology. He was a Fellow of the American College of Obstetricians and Gynecologists, the International College of Surgeons, and the American College of Surgeons. His memberships included the Academy of Medicine, the Niagara County Medical Society, and the Medical Society of the State of New York.

Joseph James Guarrera, MD, Fulton. Died September 6, 1992; age 61. Dr Guarrera was a 1956 graduate of the State University of New York Upstate Medical Center, Syracuse. He was a Diplomate of the American Board of Family Practice. His memberships included the Oswego County Medical Society and the Medical Society of the State of New York.

C. Saloman Joller, MD, Bronx. Died March 13, 1992; age 83. Dr Joller was a 1937 graduate of Deutsche Universität Medizinische Fakultät, Prag. He was a Diplomate of the American Board of Family Practice. He was a Fellow of the American Academy of Family Practice. His memberships included the Bronx County Medical Society and the Medical Society of the State of New York.

Ill Soo Kim, MD, Pittsford. Died September 18, 1992; age 50. Dr Kim was a 1967 graduate of Yonsei University College of Medicine-Severance Union Medical College. He was a Diplomate of the American Board of Radiology. His memberships included the Monroe County Society and the Medical Society of the State of New York.

Emanuel Krinsky, MD, Cedarhurst. Died July 29, 1992; age 94. Dr Krinsky was a 1921 graduate of Columbia University College of Physicians and Surgeons, New York. He was a Diplomate of the American Board of Ophthalmology. His memberships included the Academy of Medicine, the American Academy of Ophthalmology and Otolaryngology, the Aerospace Medical Association, the Kings County Medical

Society, and the Medical Society of the State of New York.

Peter Lacovara, MD, Flushing. Died March 1, 1992; age 81. Dr Lacovara was a 1937 graduate of St Louis University School of Medicine. His memberships included the Queens County Medical Society and the Medical Society of the State of New York.

Wesley Edgar Leonard, MD, Concord, New Hampshire. Died July 20, 1992; age 75. Dr Leonard was a 1942 graduate of the John Hopkins University School of Medicine, Baltimore, Maryland. He was a Fellow of the American Academy of Family Practice. His memberships included the Nassau County Medical Society and the Medical Society of the State of New York.

Albert Lesser, MD, Rockville, Maryland. Died August 18, 1992; age 85. Dr Lesser was a 1931 graduate of New York Medical College. He was a Diplomate of the American Board of Surgery. He was a Fellow of the American College of Surgeons. His memberships included the Nassau County Medical Society and the Medical Society of the State of New York.

Imre Ligeti, MD, Princeton Junction, New Jersey. Died July 30, 1992; age 80. Dr Ligeti was a 1936 graduate of Szegei Tudományegyetem Orvostudományi Fakultás, Szeged. His memberships included the Suffolk County Medical Society and the Medical Society of the State of New York.

Theodore Mandelbaum, MD, Tenafly, New Jersey. Died September 2, 1992; age 84. Dr Mandelbaum was a 1935 graduate of New York University College of Medicine, New York. He was a Diplomate of the American Board of Internal Medicine. He was a Fellow of the American College of Physicians and the American College of Cardiology. His memberships included the Academy of Medicine, the New York State Society of Internal Medicine, the International Society of Internal Medicine, the American Thoracic Society, the American Society of Internal Medicine, the Nassau County Medical Society, and the Medical Society of the State of New York.

William McDonald Jr, MD, Cohoes. Died April 13, 1992; age 48. Dr McDonald was a 1992 graduate of the Albany Medical College of Union University. He was a Diplomate of the American Board of Urology. His memberships included the American Urological Association, the Albany County Medical Society, and the Medical Society of the State of New York.

Jose Mijangos, MD, Rochester. Died July 24, 1992; age 49. Dr Mijangos was a 1968 graduate of Universidad Nacional Autónoma de México Facultad de Medicina, México. He was a Diplomate of the American Board of Surgery and the American Board of Thoracic Surgery. His memberships included the Monroe County

Medical Society and the Medical Society of the State of New York.

Mario Milazzo, MD, Freeport. Died October 8, 1992; age 67. Dr Milazzo was a 1950 graduate of Università Degli Studi Di Catania, Facoltà Di Medicina E Chirurgia. He was a Fellow of the American Academy of Family Practice. His memberships included the Pan American Medical Association, the Nassau County Medical Society, and the Medical Society of the State of New York.

James Joseph O'Rourke, MD, Yonkers. Died April 28, 1992; age 75. Dr O'Rourke was a 1943 graduate of New York Medical College. He was a Diplomate of the American Board of Obstetrics and Gynecology. His memberships included the New York County Medical Society and the Medical Society of the State of New York.

Nello Nepola, MD, Staten Island. Died September 23, 1992; age 80. Dr Nepola was a 1940 graduate of the St Louis University School of Medicine, Missouri. He was a Fellow of the International College of Surgeons and the American College of Surgeons. His memberships included the Richmond County Medical Society and the Medical Society of the State of New York.

Richard C. Packert, MD, New York. Died July 31, 1992; age 67. Dr Packert was a 1952 graduate of Tufts University School of Medicine, Boston, Massachusetts. He was a Diplomate of the American Board of Radiology. His memberships included the New York Roentgen Society, the New York County Medical Society, and the Medical Society of the State of New York.

Neil M. Palladino, MD, Levittown. Died September 30, 1992; age 65. Dr Palladino was a 1951 graduate of Harvard Medical School, Boston, Massachusetts. He was a Diplomate of the American Board of Pediatrics. He was a Fellow of the American Academy of Pediatrics. His memberships included the Nassau County Medical Society and the Medical Society of the State of New York.

Isaac Perera, MD, New York. Died July 17, 1992; age 58. Dr Perera was a 1961 graduate of the Universidad De Chile Facultad De Ciencias Medicas Santiago. His memberships included the Westchester County Medical Society and the Medical Society of the State of New York.

Nessim Jack Romano, MD, Forest Hills. Died August 19, 1992; age 67. Dr Romano was a 1950 graduate of Foad First University Faculty of Medicine, Cairo. He was a Diplomate of the American Board of Family Practice. He was a Fellow of the American Academy of Family Practice. His memberships included the American Geriatrics Society, the Queens County Medical Society, and the Medical Society of the State of New York.

Samuel A. Rosenberg, MD, Brooklyn. Died August 11, 1992; age 77. Dr Rosenberg was a 1938 graduate of the State University of New York Health Science Center at Brooklyn. He was a Diplomate of the American Board of Ophthalmology. He was a Fellow of the American College of Surgeons. His memberships included the Kings County Medical Society and the Medical Society of the State of New York.

Henry Rosner, MD, Brooklyn. Died September 15, 1992; age 85. Dr Rosner was a 1933 graduate of Creighton University School of Medicine, Omaha, Nebraska. He was a Diplomate of the American Board of Physical Medicine and Rehabilitation. His memberships included the New York Society for Physical Medicine and Rehabilitation, the American Academy of Family Practice, the American Academy of Physical Medicine and Rehabilitation, the Kings County Medical Society, and the Medical Society of the State of New York.

Abraham J. Schechter, MD, Los Angeles, California. Died August 20, 1992; age 86. Dr Schechter was a 1931 graduate of Yale University School of Medicine, New Haven, Connecticut. He was a Diplomate of the American Board of Radiology. His memberships included the Kings County Medical Society and the Medical Society of the State of New York.

Robert H Semlear, Sr, MD, East Hampton. Died September 7, 1992; age 70. Dr Semlear was a 1951 graduate of Temple University School of Medicine, Philadelphia, Pennsylvania. He was a Diplomate of the American Board of Family Practice. His memberships included the Suffolk County Medical Society and the Medical Society of the State of New York.

Fred Shalwitz, MD, Buffalo. Died July 29, 1992; age 77. Dr Shalwitz was a 1949 graduate of the University of Buffalo School of Medicine. He was a Diplomate of the American Board of Family Practice. His memberships included the Erie County Medical Society and the Medical Society of the State of New York.

Hamilton D. Soden, MD, Brooklyn. Died September 3, 1992; age 89. Dr Soden was a 1935 graduate of Howard University College of Medicine, Washington. His memberships included the New York Cardiological Society, the Kings County Medical Society, and the Medical Society of the State of New York.

Walter Solomon, MD, Staten Island. Died August 17, 1992; age 79. Dr Solomon was a 1937 graduate of New York University College of Medicine. He was a Diplomate of the American Board of Internal Medicine. He was a Fellow of the American College of Physicians. His memberships included the Academy of Medicine, the Richmond County Medical Society, and

the Medical Society of the State of New York.

Julius J. Stein, MD, New York. Died August 4, 1992; age 73. Dr Stein was a 1946 graduate of the New York Medical College, Flower and Fifth Ave Hospitals. He was a Diplomate of the American Board of Internal Medicine. His memberships included the New York State Society of Internal Medicine, the American Geriatrics Society, the New York County Medical Society, and the Medical Society of the State of New York.

Franklin F. Teller, MD, Farmingdale. Died September 25, 1992; age 72. Dr Teller was a 1945 graduate of Middlesex University School of Medicine, Waltham, Massachusetts. He was a Diplomate of the American Board of Internal Medicine. His memberships included the New York Society of Internal Medicine, the American Society of Internal Medicine, the Nassau County

Medical Society, and the Medical Society of the State of New York.

Alton Bernard Thompson, MD, Pulaski. Died March 6, 1992; age 66. Dr Thompson was a 1930 graduate of the State University of New York Upstate Medical Center, Syracuse. His memberships included the American Academy of Family Practice, the Oswego County Medical Society, and the Medical Society of the State of New York.

Joseph F. Valicenti, MD, Elmira. Died August 28, 1992; age 84. Dr Valicenti was a 1939 graduate of Georgetown University School of Medicine. His memberships included the American Academy of Family Practice, the Chemung County Medical Society, and the Medical Society of the State of New York.

George Van Sonnenberg, MD, Ardsley. Died September 7, 1992; age 80. Dr Van Sonnenberg was a 1937 graduate of Univer-

sita Degli Studi Di Siena, Facolta Di Medicina E Chirurgia. His memberships included the American Geriatrics Society, the Bronx County Medical Society, and the Medical Society of the State of New York.

Maria Wenzl, MD, Rochester. Died July 12, 1992; age 85. Dr Wenzl was a 1932 graduate of Medizinische Fakultat Der Universitat, Wein, Germany. She was a Fellow of the American College of Chest Physicians. Her memberships included the American Thoracic Society, the Monroe County Medical Society, and the Medical Society of the State of New York.

Joshua F. Zendel, MD, Eastchester. Died July 5, 1992; age 84. Dr Zendel was a 1932 graduate of the New York University College of Medicine. He was a Diplomate of the American Board of Internal Medicine. His memberships included the Academy of Medicine, the New York County Medical Society, and the Medical Society of the State of New York.

Our referees

The cornerstone of a peer-reviewed journal is its refereeing process. In 1992 the individuals listed below served as referees for manuscripts submitted to the Journal. Their continuing contribution is acknowledged with deep appreciation.

Jay M. Aggarwal, MD, Raytown, MO
Charles Alcorn, ScD, Lake Success, NY
Antonio E. Alfonso, MD, Brooklyn, NY
George Annas, JD, Boston, MA
Oscar Auerbach, MD, East Orange, NJ
Alberto G. Ayala, MD, Houston, TX
Robert J. Bache, MD, Minneapolis, MN
J. David Beatty, MD, Toronto, Ontario
Gary B. Beringer, D^{PH}, White Plains, NY
Julian L. Berman, MD, Coral Springs, FL
Thomas M. Biancaniello, MD, Stony Brook, NY
William Bilnoski, MD, Auburn, WA
Naomi Bluestone, MD, Center Barnstead, NH
Sharon Blumer, MS, Atlanta, GA
Ben Boal, MD, Jamaica, NY
John Boyce, MD, Brooklyn, NY
Robert D. Brandstetter, MD, New Rochelle, NY
Peter J. Buchin, MD, New York, NY
Billy E. Buck, MD, South Miami, FL
Richard Calame, MD, Brooklyn, NY
Jorge L. Camunas, MD, New York, NY
Hugh Carroll, MD, Brooklyn, NY
Robert Caruso, MD, Jamaica, NY
Alexander E. Chang, MD, Ann Arbor, MI
Dennis J. Cleri, MD, Paterson, NJ
Lawrence H. Clouse, MD, Marshfield, WI
Hartley Cohen, MD, Los Angeles, CA
Barry S. Collier, MD, Stony Brook, NY
Christopher J. Cooper, MD, Boston, MA
Adnan S. Dajani, MD, Detroit, MI
David C. Dale, MD, Seattle, WA
Jack A. DeHovitz, MD, Brooklyn, NY
Jeffrey C. Delafuente, MS, Gainesville, FL
Thomas Logan Dent, MD, Abington, PA
Vincent T. DeVita, MD, New York, NY
Gordon M. Dickinson, Jr, MD, Miami, FL
George DiFerdinando, MD, Albany, NY
Donald B. Doty, MD, Salt Lake City, UT
Stephen C. Dreskin, MD, Denver, CO
Lewis C. Drusin, MD, New York, NY
Michael England, MD, St Paul, MN
Howard S. Faden, MD, Buffalo, NY
Joseph Feldman, D^{PH}, Brooklyn, NY
Charles M. Ferguson, MD, Atlanta, GA
Jay Fleisher, MD, Brooklyn, NY
Arthur Fox, MD, New York, NY
Roger A. Freedman, MD, Salt Lake City, UT
Paul Froom, MD, Menashe, Israel
Osvaldo J. Fulco, MD, East Meadow, NY
Wayne L. Furman, MD, Memphis, TN
David Gerber, MD, Atlanta, GA
Charles Gerson, MD, New York, NY
Eli Ginzberg, PhD, New York, NY

Martin S. Gizzi, MD, New York, NY
Eli S. Goldensohn, MD, Nyack, NY
Sherwin Goldman, MD, Rochester, MN
Gerald Gollen, MD, New Haven, CT
Ernesto Gonzalez, MD, Boston, MA
Helmut Haas, MD, Portland, OR
John D. Hainsworth, MD, Nashville, TN
John S. Haller, Jr, PhD, Carbondale, IL
Brian C. Halpern, MD, Princeton, NJ
Bette M. Harig, MD, New York, NY
John B. Harley, MD, Oklahoma City, OK
Bruce A. Harms, MD, Madison, WI
John G. Harold, MD, Los Angeles, CA
Barry J. Hartman, MD, New York, NY
Donald B. Hawkins, MD, Los Angeles, CA
June A. Heitmann, MD, New York, NY
Charles B. Hicks, MD, McLean, VA
Susan Hilton, MD, New York, NY
Linda B. Hiner, MD, Philadelphia, PA
Sally Hipp, PhD, Albany, NY
Charles R. Horsburgh, Jr, MD, Atlanta, GA
Verne L. Hoshal, Jr, MD, Ann Arbor, MI
Donald Hoskins, MD, New York, NY
Vincent J. Hyams, MD, Silver Springs, MD
Nicholas O. Iannotti, MD, Port St Lucie, FL
Suzanne Ildstad, MD, Pittsburgh, PA
Bruce E. Jarrell, MD, Philadelphia, PA
Richard Kanner, MD, Salt Lake City, UT
James R. Kassen, MD, Boston, MA
Alvin Katz, MD, New York, NY
Mary M. Kemeny, MD, New York, NY
David W. Kinne, MD, New York, NY
David Klot, MD, Brooklyn, NY
Virginia Ktsanes, PhD, New Orleans, LA
Mortimer Lacher, MD, New York, NY
Herbert Lepor, MD, Milwaukee, WI
Carlos Li, MD, Los Angeles, CA
Marcia K. Liepman, MD, East Douglas, MA
Toby L. Litovitz, MD, Potomac, MD
Richard R. Love, MD, Madison, WI
Harvinder Luthra, MD, Rochester, MN
Yela L. Lynfield, MD, Cederhurst, NY
Thomas E. MacGillivray, MD, Boston, MA
Adel Z. Makary, MD, Danville, PA
Lois Y. Matsuoka, MD, Philadelphia, PA
Kenneth L. Mattox, MD, Houston, TX
Peter P. McKellar, MD, Paradise Valley, AZ
Charles K. McSherry, MD, New York, NY
Rabbi Levi Meier, PhD, Los Angeles, CA
Mickey S. Meiselman, MD, Evanston, IL
Stacey E. Mills, MD, Charlottesville, VA
Howard L. Minkoff, MD, Far Rockaway, NY
Thomas Monahan, Albany, NY

Jonathan Moreno, PhD, Brooklyn, NY
John H. Morton, MD, Rochester, NY
Henry Murray, MD, New York, NY
Daniel M. Musher, MD, Houston, TX
Alfred I. Neugut, MD, New York, NY
Stephen Nordlicht, MD, New York, NY
Neil J. Nusbaum, MD, Brooklyn, NY
David D. Oakes, MD, Atherton, CA
John T. Parente, MD, Manhasset, NY
Harold L. Paz, MD, Philadelphia, PA
Daniel L. Picard, MD, Flushing, NY
Vincent Pillari, MD, Staten Island, NY
Warren C. Plauche, MD, Harahan, LA
Daniel D. Rabuzzi, MD, Syracuse, NY
John Ranson, MD, New York, NY
Rayasam H. Rao, MD, Pittsburgh, PA
Aaron P. Rapoport, MD, Rochester, NY
Kenneth Raske, MD, New York, NY
Frank Redo, MD, New York, NY
Arthur L. Reingold, MD, Berkeley, CA
Ronald Rieder, MD, Brooklyn, NY
Leslie Rocher, MD, Royal Oaks, MI
P. Peter Rosen, MD, New York, NY
David G. Rustad, MD, Minneapolis, MN
Ralph L. Sacco, MD, New York, NY
Samuel A. Santoro, MD, St Louis, MO
Jeffrey S. Sartin, MD, Andrews AFB, MD
Peter M. Schantz, MD, Atlanta, GA
Joseph Schluger, MD, New York, NY
Theodore Schussler, MD, Brooklyn, NY
Archie Silver, MD, Tampa, FL
Frederick A. Simeone, MD, Philadelphia, PA
Anthony Sossi, MD, Jamaica, NY
Thomas R. Stevenson, MD, Saramento, CA
Henry G. Stratmann, MD, St Louis, MO
Raphael P. Stricker, MD, San Francisco, CA
Steven Stylianos, MD, Boston, MA
Paul S. Swaye, MD, Miami Beach, FL
Andrew J. Swinburne, MD, Rochester, NY
Arthur N. Tessler, MD, New York, NY
Michael F. Tenholder, MD, Augusta, GA
Seth R. Thaller, MD, Sacramento, CA
Joseph D. Tobias, MD, Nashville, TN
Paul A. Tunick, MD, New York, NY
Rodrigo Urizar, MD, Loudonville, NY
Ronald Valdiserri, MD, Atlanta, GA
Dennis D. Venable, MD, Shreveport, LA
Irene L. Wapnir, MD, New Brunswick, NJ
Raymond G. Watts, MD, Birmingham, AL
Irwin M. Weiner, MD, Brooklyn, NY
Richard Wernick, MD, Portland, OR
Donald E. Wesson, MD, Houston, TX
Sidney J. Winawer, MD, New York, NY

Reference: 1. Jones PH, et al. Once-daily pravastatin in patients with primary hypercholesterolemia: a dose-response study. *Clin Cardiol*. 1991;14:146-151.

PRAVACHOL® (Pravastatin Sodium Tablets)

CONTRAINDICATIONS

Hypersensitivity to any component of this medication.

Active liver disease or unexplained, persistent elevations in liver function tests (see WARNINGS).

Pregnancy and lactation. Atherosclerosis is a chronic process and discontinuation of lipid-lowering drugs during pregnancy should have little impact on the outcome of long-term therapy of primary hypercholesterolemia. Cholesterol and other products of cholesterol biosynthesis are essential components for fetal development (including synthesis of steroids and cell membranes). Since HMG-CoA reductase inhibitors decrease cholesterol synthesis and possibly the synthesis of other biologically active substances derived from cholesterol, they may cause fetal harm when administered to pregnant women. Therefore, HMG-CoA reductase inhibitors are contraindicated during pregnancy and in nursing mothers. **Pravastatin should be administered to women of childbearing age only when such patients are highly unlikely to conceive and have been informed of the potential hazards.** If the patient becomes pregnant while taking this class of drug, therapy should be discontinued and the patient apprised of the potential hazard to the fetus.

WARNINGS

Liver Enzymes: HMG-CoA reductase inhibitors, like some other lipid-lowering therapies, have been associated with biochemical abnormalities of liver function. Increases of serum transaminase (ALT, AST) values to more than 3 times the upper limit of normal occurring on 2 or more (not necessarily sequential) occasions have been reported in 1.3% of patients treated with pravastatin in the U.S. over an average period of 18 months. These abnormalities were not associated with cholestasis and did not appear to be related to treatment duration. In those patients in whom these abnormalities were believed to be related to pravastatin and who were discontinued from therapy, the transaminase levels usually fell slowly to pretreatment levels. These biochemical findings are usually asymptomatic although worldwide experience indicates that anorexia, weakness, and/or abdominal pain may also be present in rare patients.

As with other lipid-lowering agents, liver function tests should be performed during therapy with pravastatin. Serum aminotransferases, including ALT (SGPT), should be monitored before treatment begins, every six weeks for the first three months, every eight weeks during the remainder of the first year, and periodically thereafter (e.g., at about six-month intervals). Special attention should be given to patients who develop increased transaminase levels. Liver function tests should be repeated to confirm an elevation and subsequently monitored at more frequent intervals. If increases in AST and ALT equal or exceed three times the upper limit of normal and persist, then therapy should be discontinued. Persistence of significant aminotransferase elevations following discontinuation of therapy may warrant consideration of liver biopsy.

Active liver disease or unexplained transaminase elevations are contraindications to the use of pravastatin (see CONTRAINDICATIONS). Caution should be exercised when pravastatin is administered to patients with a history of liver disease or heavy alcohol ingestion (see CLINICAL PHARMACOLOGY: Pharmacokinetics/Metabolism). Such patients should be closely monitored, started at the lower end of the recommended dosing range, and titrated to the desired therapeutic effect.

Skeletal Muscle: Rhabdomyolysis with renal dysfunction secondary to myoglobinuria has been reported with pravastatin and other drugs in this class. Uncomplicated myalgia has also been reported in pravastatin-treated patients (see ADVERSE REACTIONS). Myopathy, defined as muscle aching or muscle weakness in conjunction with increases in creatine phosphokinase (CPK) values to greater than 10 times the upper limit of normal was reported to be possibly due to pravastatin in only one patient in clinical trials (<0.1%). Myopathy should be considered in any patient with diffuse myalgias, muscle tenderness or weakness, and/or marked elevation of CPK. Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever. **Pravastatin therapy should be discontinued if markedly elevated CPK levels occur or myopathy is diagnosed or suspected.** Pravastatin therapy should also be temporarily withheld in any patient experiencing an acute or serious condition predisposing to the development of renal failure secondary to rhabdomyolysis, e.g., sepsis; hypotension; major surgery; trauma; severe metabolic, endocrine, or electrolyte disorders; or uncontrolled epilepsy.

The risk of myopathy during treatment with lovastatin is increased if therapy with either cyclosporine, gemfibrozil, erythromycin, or niacin is administered concurrently. There is no experience with the use of pravastatin together with cyclosporine. Myopathy has not been observed in clinical trials involving small numbers of patients who were treated with pravastatin together with niacin. One trial of limited size involving combined therapy with pravastatin and gemfibrozil showed a trend toward more frequent CPK elevations and patient withdrawals due to musculoskeletal symptoms in the group receiving combined treatment as compared with the groups receiving placebo, gemfibrozil, or pravastatin monotherapy. Myopathy was not reported in this trial (see PRECAUTIONS: Drug Interactions). One patient developed myopathy when clofibrate was added to a previously well tolerated regimen of pravastatin; the myopathy resolved when clofibrate therapy was stopped and pravastatin treatment continued. **The use of fibrates alone may occasionally be associated with myopathy. The combined use of pravastatin and fibrates should generally be avoided.**

PRECAUTIONS

General: Pravastatin may elevate creatine phosphokinase and transaminase levels (see ADVERSE REACTIONS). This should be considered in the differential diagnosis of chest pain in a patient on therapy with pravastatin.

Homozygous Familial Hypercholesterolemia. Pravastatin has not been evaluated in patients with rare homozygous familial hypercholesterolemia. In this group of patients, it has been reported that HMG-CoA reductase inhibitors are less effective because the patients lack functional LDL receptors.

Renal Insufficiency. A single 20 mg oral dose of pravastatin was administered to 24 patients with varying degrees of renal impairment (as determined by creatinine clearance). No effect was observed on the pharmacokinetics of pravastatin or its 3 α -hydroxy isomeric metabolite (SQ 31,906). A small increase was seen in mean AUC values and half-life (t_{1/2}) for the inactive enzymatic ring hydroxylation metabolite (SQ 31,945). Given this small sample size, the dosage administered, and the degree of individual variability, patients with renal impairment who are receiving pravastatin should be closely monitored.

Information for Patients: Patients should be advised to report promptly unexplained muscle pain, tenderness or weakness, particularly if accompanied by malaise or fever.

Drug Interactions: Immunosuppressive Drugs, Gemfibrozil, Niacin (Nicotinic Acid), Erythromycin. See WARNINGS: Skeletal Muscle.

Antipyrine: Clearance by the cytochrome P450 system was unaltered by concomitant administration of pravastatin. Since pravastatin does not appear to induce hepatic drug-metabolizing enzymes, it is not expected that any significant interaction of pravastatin with other drugs (e.g., phenytoin, quinidine) metabolized by the cytochrome P450 system will occur.

Cholestyramine/Colestipol: Concomitant administration resulted in an approximately 40 to 50% decrease in the mean AUC of pravastatin. However, when pravastatin was administered 1 hour before or 4 hours after cholestyramine or 1 hour before colestipol and a standard meal, there was no clinically significant decrease in bioavailability or therapeutic effect. (See DOSAGE AND ADMINISTRATION: Concomitant Therapy.)

Warfarin: In a study involving 10 healthy male subjects given pravastatin and warfarin concomitantly for 6 days, bioavailability parameters at steady state for pravastatin (parent compound) were not altered. Pravastatin did not alter the plasma protein-binding of warfarin. Concomitant dosing did increase the AUC and C_{max} of warfarin but did not produce any changes in its anticoagulant action (i.e., no increase was seen in mean prothrombin time after 6 days of concomitant therapy). However, bleeding and extreme prolongation of prothrombin time has been reported with another drug in this class. Patients receiving warfarin-type anticoagulants should have their prothrombin times closely monitored when pravastatin is initiated or the dosage of pravastatin is changed.

Cimetidine: The AUC_{0-12h} for pravastatin when given with cimetidine was not significantly different from the AUC for pravastatin when given alone. A significant difference was observed between the AUC's for pravastatin when given with cimetidine compared to when administered with antacid.

Digoxin: In a crossover trial involving 18 healthy male subjects given pravastatin and digoxin concurrently for 9 days, the bioavailability parameters of digoxin were not affected. The AUC of pravastatin tended to increase, but the overall bioavailability of pravastatin plus its metabolites SQ 31,906 and SQ 31,945 was not altered.

Gemfibrozil: In a crossover study in 20 healthy male volunteers given concomitant single doses of pravastatin and gemfibrozil, there was a significant decrease in urinary excretion and protein binding of pravastatin. In addition, there was a significant increase in AUC, C_{max}, and T_{max} for the pravastatin metabolite SQ 31,906. Combination therapy with pravastatin and gemfibrozil is generally not recommended.

In interaction studies with aspirin, antacids [1 hour prior to PRAVACHOL (pravastatin sodium)], cimetidine, nicotinic acid, or probucol, no statistically significant differences in bioavailability were seen when PRAVACHOL was administered.

Other Drugs: During clinical trials, no noticeable drug interactions were reported when PRAVACHOL was added to: diuretics, antihypertensives, digitalis, converting-enzyme inhibitors, calcium channel blockers, beta-blockers, or nitroglycerin.

Endocrine Function: HMG-CoA reductase inhibitors interfere with cholesterol synthesis and lower circulating cholesterol levels and, as such, might theoretically blunt adrenal or gonadal steroid hormone production. Results of clinical trials with pravastatin in males and post-menopausal females were inconsistent with regard to possible effects of the drug on basal steroid hormone levels. In a study of 21 males, the mean testosterone response to human chorionic gonadotropin was significantly reduced (p<0.004) after 16 weeks of treatment with 40 mg of pravastatin. However, the percentage of patients showing a $\geq$ 50% rise in plasma testosterone after human chorionic gonadotropin stimulation did not change significantly after therapy in these patients. The effects of HMG-CoA reductase inhibitors on spermatogenesis and fertility have not been studied in adequate numbers of patients. The effects, if any, of pravastatin on the pituitary-gonadal axis in pre-menopausal females are unknown. Patients treated with pravastatin who display clinical evidence of endocrine dysfunction should be evaluated appropriately. Caution should also be exercised if an HMG-CoA reductase inhibitor or other agent used to lower cholesterol levels is administered to patients also receiving other drugs (e.g., ketoconazole, spironolactone, cimetidine) that may diminish the levels or activity of steroid hormones.

CNS Toxicity: CNS vascular lesions, characterized by perivascular hemorrhage and edema and mononuclear cell

infiltration of perivascular spaces, were seen in dogs treated with pravastatin at a dose of 25 mg/kg/day, a dose that produced a plasma drug level about 50 times higher than the mean drug level in humans taking 40 mg/day. Similar CNS vascular lesions have been observed with several other drugs in this class.

A chemically similar drug in this class produced optic nerve degeneration (Wallenian degeneration of retinoculinate fibers) in clinically normal dogs in a dose-dependent fashion starting at 60 mg/kg/day, a dose that produced mean plasma drug levels about 30 times higher than the mean drug level in humans taking the highest recommended dose (as measured by total enzyme inhibitory activity). This same drug also produced vestibulocochlear Wallenian-like degeneration and retinal ganglion cell chromatolysis in dogs treated for 14 weeks at 180 mg/kg/day, a dose which resulted in a mean plasma drug level similar to that seen with the 60 mg/kg dose.

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a 2-year study in rats fed pravastatin at doses of 10, 30, or 100 mg/kg body weight, there was an increased incidence of hepatocellular carcinomas in males at the highest dose (p<0.01). Although rats were given up to 125 times the human dose (HD) on a mg/kg body weight basis, their serum drug levels were only 6 to 10 times higher than those measured in humans given 40 mg pravastatin as measured by AUC.

The oral administration of 10, 30, or 100 mg/kg (producing plasma drug levels approximately 0.5 to 5.0 times human drug levels at 40 mg) of pravastatin to mice for 22 months resulted in a statistically significant increase in the incidence of malignant lymphomas in treated females when all treatment groups were pooled and compared to controls (p<0.05). The incidence was not dose-related and male mice were not affected.

A chemically similar drug in this class was administered to mice for 72 weeks at 25, 100, and 400 mg/kg body weight, which resulted in mean serum drug levels approximately 3, 15, and 33 times higher than the mean human serum drug concentration (as total inhibitory activity) after a 40 mg oral dose. Liver carcinomas were significantly increased in high-dose females and mid- and high-dose males, with a maximum incidence of 90 percent in males. The incidence of adenomas of the liver was significantly increased in mid- and high-dose females. Drug treatment also significantly increased the incidence of lung adenomas in mid- and high-dose males and females. Adenomas of the eye Harderian gland (a gland of the eye of rodents) were significantly higher in high-dose mice than in controls.

No evidence of mutagenicity was observed *in vitro*, with or without rat-liver metabolic activation, in the following studies: microbial mutagen tests, using mutant strains of *Salmonella typhimurium* or *Escherichia coli*, a forward mutation assay in L5178Y TK +/– mouse lymphoma cells; a chromosomal aberration test in hamster cells, and a gene conversion assay using *Saccharomyces cerevisiae*. In addition, there was no evidence of mutagenicity in either a dominant lethal test in mice or a micronucleus test in mice.

In a study in rats, with daily doses up to 500 mg/kg, pravastatin did not produce any adverse effects on fertility or general reproductive performance. However, in a study with another HMG-CoA reductase inhibitor, there was decreased fertility in male rats treated for 34 weeks at 25 mg/kg body weight, although this effect was not observed in a subsequent fertility study when this same dose was administered for 11 weeks (the entire cycle of spermatogenesis, including epididymal maturation). In rats treated with this same reductase inhibitor at 180 mg/kg/day, seminiferous tubule degeneration (necrosis and loss of spermatogenic epithelium) was observed. Although not seen with pravastatin, two similar drugs in this class caused drug-related testicular atrophy, decreased spermatogenesis, spermatocytic degeneration, and giant cell formation in dogs. The clinical significance of these findings is unclear.

Pregnancy: Pregnancy Category X: See CONTRAINDICATIONS.

Safety in pregnant women has not been established. Pravastatin was not teratogenic in rats at doses up to 1000 mg/kg daily or in rabbits at doses of up to 50 mg/kg daily. These doses resulted in 20x (rabbit) or 240x (rat) the human exposure based on surface area (mg/m²). However, in studies with another HMG-CoA reductase inhibitor, skeletal malformations were observed in rats and mice. PRAVACHOL (pravastatin sodium) should be administered to women of child-bearing potential only when such patients are highly unlikely to conceive and have been informed of the potential hazards. If the woman becomes pregnant while taking PRAVACHOL, it should be discontinued and the patient advised again as to the potential hazards to the fetus.

Nursing Mothers: A small amount of pravastatin is excreted in human breast milk. Because of the potential for serious adverse reactions in nursing infants, women taking PRAVACHOL should not nurse (see CONTRAINDICATIONS).

Pediatric Use: Safety and effectiveness in individuals less than 18 years old have not been established. Hence, treatment in patients less than 18 years old is not recommended at this time. (See also PRECAUTIONS: General.)

ADVERSE REACTIONS

Pravastatin is generally well tolerated; adverse reactions have usually been mild and transient. In 4-month long placebo-controlled trials, 1.7% of pravastatin-treated patients and 1.2% of placebo-treated patients were discontinued from treatment because of adverse experiences attributed to study drug therapy, this difference was not statistically significant. In long-term studies, the most common reasons for discontinuation were asymptomatic serum transaminase increases and mild, non-specific gastrointestinal complaints. During clinical trials the overall incidence of adverse events in the elderly was not different from the incidence observed in younger patients.

Adverse Clinical Events: All adverse clinical events (regardless of attribution) reported in more than 2% of pravastatin-treated patients in the placebo-controlled trials are identified in the table below; also shown are the percentages of patients in whom these medical events were believed to be related or possibly related to the drug:

Body System/Event	All Events %		Events Attributed to Study Drug %	
	Pravastatin (N = 900)	Placebo (N = 411)	Pravastatin (N = 900)	Placebo (N = 411)
Cardiovascular				
Cardiac Chest Pain	4.0	3.4	0.1	0.0
Dermatologic				
Rash	4.0*	1.1	1.3	0.9
Gastrointestinal				
Nausea/Vomiting	7.3	7.1	2.9	3.4
Diarrhea	6.2	5.6	2.0	1.9
Abdominal Pain	5.4	6.9	2.0	3.9
Constipation	4.0	7.1	2.4	5.1
Flatulence	3.3	3.6	2.7	3.4
Heartburn	2.9	1.9	2.0	0.7
General				
Fatigue	3.8	3.4	1.9	1.0
Chest Pain	3.7	1.9	0.3	0.2
Influenza	2.4*	0.7	0.0	0.0
Musculoskeletal				
Localized Pain	10.0	9.0	1.4	1.5
Myalgia	2.7	1.0	0.6	0.0
Nervous System				
Headache	6.2	3.9	1.7*	0.2
Dizziness	3.3	3.2	1.0	0.5
Renal/Genitourinary				
Urinary Abnormality	2.4	2.9	0.7	1.2
Respiratory				
Common Cold	7.0	6.3	0.0	0.0
Rhinitis	4.0	4.1	0.1	0.0
Cough	2.6	1.7	0.1	0.0

*Statistically significantly different from placebo.

The following effects have been reported with drugs in this class:

Skeletal: myopathy, rhabdomyolysis.

Neurological: dysfunction of certain cranial nerves (including alteration of taste, impairment of extra-ocular movement, facial paresis), tremor, vertigo, memory loss, paresthesia, peripheral neuropathy, peripheral nerve palsy.

Hypersensitivity Reactions: An apparent hypersensitivity syndrome has been reported rarely which has included one or more of the following features: anaphylaxis, angioedema, lupus erythematosus-like syndrome, polymyalgia rheumatica, vasculitis, purpura, thrombocytopenia, leukopenia, hemolytic anemia, positive ANA, ESR increase, arthritis, arthralgia, urticaria, asthenia, photosensitivity, fever, chills, flushing, malaise, dyspnea, toxic epidermal necrolysis, erythema multiforme, including Stevens-Johnson syndrome.

Gastrointestinal: pancreatitis, hepatitis, including chronic active hepatitis, cholestatic jaundice, fatty change in liver, and, rarely, cirrhosis, fulminant hepatic necrosis, and hepatoma, anorexia, vomiting.

Reproductive: gynecostasia, loss of libido, erectile dysfunction.

Eye: progression of cataracts (lens opacities), ophthalmoplegia.

Laboratory Test Abnormalities: Increases in serum transaminase (ALT, AST) values and CPK have been observed (see WARNINGS).

Transient, asymptomatic eosinophilia has been reported. Eosinophil counts usually returned to normal despite continued therapy. Anemia, thrombocytopenia, and leukopenia have been reported with other HMG-CoA reductase inhibitors.

Concomitant Therapy: Pravastatin has been administered concurrently with cholestyramine, colestipol, nicotinic acid, probucol and gemfibrozil. Preliminary data suggest that the addition of either probucol or gemfibrozil to therapy with lovastatin or pravastatin is not associated with greater reduction in LDL cholesterol than that achieved with lovastatin or pravastatin alone. No adverse reactions unique to the combination or in addition to those previously reported for each drug alone have been reported. Myopathy and rhabdomyolysis (with or without acute renal failure) have been reported when another HMG-CoA reductase inhibitor was used in combination with immunosuppressive drugs, gemfibrozil, erythromycin, or lipid-lowering doses of nicotinic acid. Concomitant therapy with HMG-CoA reductase inhibitors and these agents is generally not recommended (See WARNINGS: Skeletal Muscle and PRECAUTIONS: Drug Interactions.)

OVERDOSAGE

There have been no reports of overdoses with pravastatin.

Should an accidental overdose occur, treat symptomatically and institute supportive measures as required.

THE PRAVACHOL® DIRECTION
IN LIPID MANAGEMENT

Effective lipid management doesn't have to be tough



- Improves key lipids — significant reduction in LDL-C¹
- Excellent safety profile
- Easy for patients — once-daily dosing, well tolerated
- Usual dose: 20 mg once daily at bedtime, with or without food


PRAVACHOL®
pravastatin sodium 20 mg tablets

PRAVACHOL is indicated as an adjunct to diet for the reduction of elevated total and LDL-cholesterol levels in patients with primary hypercholesterolemia (Types IIa and IIb) when the response to diet alone has not been adequate.

Active liver disease or unexplained transaminase elevations, pregnancy and lactation are contraindications to the use of pravastatin sodium.

Please see CONTRAINDICATIONS, WARNINGS, PRECAUTIONS, and ADVERSE REACTIONS in the brief summary of prescribing information on the adjacent page.



Bristol-Myers Squibb Company

THE NEW YORK ACADEMY
OF MEDICINE



This BOOK
is NOT to be REMOVED
from the LIBRARY

NEW YORK ACADEMY OF MEDICINE



3 0681 0131984 4

